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POSITION OF MUSCLES AFTER OPERATION FOR STRABISMUS

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Among surgeons operating for strabismus no agreement has yet been reached concerning certain questions which are of importance in the choice of operation. Almost every operator has, for reasons which seem good to him, fixed his preference on two or at most three operations. He has obtained a fair average of results with these and, in considering the factors involved, tends to accept a theory which favors the operation of his choice. Reminiscent of the former battles between the advocates of tenotomy and those of advancement is the more recent argument between the late Dr. Jameson and Dr. O'Connor on the virtues of recession versus those of cinch shortening with central tenotomy. Worth, Landolt and their followers insist on the value of advancement with the idea that the insertion of the muscle is placed nearer the cornea, while van der Hoeve, Lancaster and others are firmly convinced that the muscle adheres to its old insertion after advancement and that this operation has, therefore, no advantage over the supposedly safer resection with attachment to the muscle stump.

It would seem that opportunity would have been afforded, during the many years in which operations for strabismus have been performed, for definite observations bearing on these points. A search of the literature, however, reveals remarkably little useful evidence. The standard works of Peter, Worth and Landolt on the extraocular muscles fail to quote any cases in which the actual position of the muscles was confirmed after operation. Van der Hoeve,[1] discussing the relative value of resection and advancement, gave some references, a few of which proved to be of interest although they concern individual observations. Wells,[2]

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1. van der Hoeve, J.: Operationslehre, in Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1922, vol. 2, p. 1645.

2. Wells, D. W.: Tr. Am. Acad. Ophth. **26**:105, 1921.

for example, exposed an external rectus muscle on which he had performed advancement with partial but insufficient result. It was found inserted 3 mm. from the limbus. Fröhlich [3] exposed the muscle five weeks after advancement and found it adherent to its old insertion. He carefully divided all the subconjunctival tissue on the limbal side of the insertion, including some muscle fibers, and found that this produced no change in the position of the eye. Hence he felt convinced that the muscle was acting entirely from its old insertion. Freiberger [4] performed recession on an eye which was to be enucleated two weeks later. He found the muscle firmly adherent over a normal area at the site of the suture. Müller [5] in a case of overeffect following tenotomy found an attachment of normal extent 4 to 5 mm. behind the original insertion, while in another case only the upper border of the tendon was adherent to the sclera.

Correspondence with Dr. Walter Lancaster revealed no pertinent articles. Dr. Luther Peter knew of none but emphasized the troublesome character of adhesions found when muscles previously operated on are exposed. He also stated: "Tenotomies, especially of the internal rectus, are poorly attached excepting for the capsule adhesions."

Dr. O'Connor stated that he had exposed the muscle in many cases after a previous operation. He had seen only 1 case in which the tendon had not become attached to the globe. After advancement he has seen "adhesions so far back behind the equator that they could not be separated." Previously he [6] had described a case in which a tenotomy of the internal rectus muscle had been performed on one eye and a recession of 3 mm. on the other. Adduction was 45 degrees on the tenotomized side but only 25 degrees on the other, indicating adhesions to the globe far back of the intended attachment. In 4 cases of divergence secondary to recession he exposed the muscle previously operated on and measured the location of its new insertion. It was 2 mm. behind the original insertion in 1 case, 3 mm. in 2 cases and 4 mm. in 1 case. In spite of this moderate change in the insertion, an overeffect with defective adduction had occurred in all cases. This was satisfactorily arrested by cinch shortenings on the muscles previously operated on.

Dr. Frederick A. Davis, after describing the precise technic of his three stitch recession, stated: "I have reoperated and found that a thickened band of tissue seems to advance forward to the original

3. Fröhlich, C.: Klin. Monatsbl. f. Augenh. **38**:369, 1900.

4. Freiberger, M.: Operation on the Ocular Muscles: A Few Points in Operative Technic, Arch. Ophth. **23**:833 (April) 1940.

5. Müller: Klin. Monatsbl. f. Augenh. **31**:118, 1893.

6. O'Connor, R.: Am. J. Ophth. **18**:1137, 1935.

incision, and thereby a good deal of the value of the recession is lost in some cases." Other observations on cases in which a second operation has been performed must have been made and may have been reported but if so are buried in articles dealing with other aspects of strabismus and hence could not be found for this review.

Apparently the only systematic attempt to apply the results of operations on animals to this problem was made by Carroll and Blake.[7] Their observations made on a large number of rabbits which were submitted to various operations are exceedingly interesting and permit some practical deductions. The animals were killed at intervals of two to forty days after operation. The location of the new attachment was noted, though not measured in most animals; its firmness was tested, and the process of healing was studied in sections. After simple tenotomy at the insertion the muscle was found attached to the sclera behind the original insertion in almost all of the animals. The exception was an animal in which resection of the opposing muscle was done at the same time; the muscle had formed no attachment to the sclera on the eighth day. In 1 animal the muscle was sectioned 4 mm. back of its insertion, and in this animal, too, no attachment had formed. During the first three weeks the attachment was by means of loose connective tissue, few muscle fibers being in actual contact with the sclera until twenty-one to forty days postoperatively. In all instances the muscle became adherent to the sclera thirteen to forty days after recession. Necrosis of muscle fibers was noted, with later absorption of the necrotic fibers. The attachment was formed by organization of fibrin and by granulation tissue. It would appear from these findings that necrosis of muscle fibers would actually shorten the muscle more than the calculated amount, while the amount of relaxation of the muscle due to the formation of granulation tissue was a variable quantity. Tucking with silk sutures was performed in 8 animals. In 1 adhesions were found between muscle and sclera 3 to 4 mm. posterior to the tuck. Such adhesions might be expected to neutralize completely the effect of the tuck and possibly to limit motion in the field of the muscle. Twelve resections were performed by the Reese technic. The resulting attachment was firm in all instances, but owing to necrosis of the muscle fibers connective tissue intervened between the muscle fibers and the sclera as late as the fortieth postoperative day. Adhesions to the sclera behind the insertion were found in several instances, so that the muscle was acting from a point 4 to 7 mm. behind its insertion. Such adhesions were due to formation of blood clots, and this factor was responsible for great variability in the resulting effective insertion of the muscle. Only

7. Carroll, F. D., and Blake, E. M.: Repair Following Operations on Extra-Ocular Muscles: Histologic Observations, Arch. Ophth. **8**:711 (April) 1932.

one advancement, by Worth's technic, was performed, and the resulting attachment showed nothing worthy of note.

Because of inability to explain certain unexpected results of operations for squint, notes have been made during the past six years on the conditions found when muscles previously operated on were exposed. For patients originally operated on by myself accurate information was available as to the type of operation and the amount of correction attempted. For some patients previously operated on elsewhere it was possible to obtain such data. For other patients it was necessary to determine the probable operation from the history or from the type of condition said to have been present for which correction was attempted. Exposure of muscles was made only when it seemed possible to correct the condition by a further surgical procedure on the muscle in question either alone or in association with an operation on its opponent. In nearly all cases the distance of the insertion from the limbus was measured with von Szily's caliper and notes were made as to irregularities in its direction or extent and of any abnormal adhesions to the sclera. When corrective procedures were performed these were noted, and the results obtained are briefly given.

The cases of muscle exposure in which such notes were made number 24. They may be classified as follows, according to the operation originally performed:

Group 1: Tenotomy, 4 cases.
Group 2: Recession, 8 cases.
Group 3: Shortening operations.
(*a*) Advancement, 1 case.
(*b*) Resection, 2 cases.
(*c*) Tucking, 1 case.
Group 4: Myotomy of the inferior oblique muscle, 2 cases.
Group 5: Tendon transplantation for abducens nerve paresis, 2 cases.
Group 6: Wiener's transplantation of the superior oblique muscle, 1 case.
Group 7: Exposure of muscle to relieve diplopia following a detachment operation, 3 cases.

Two patients appear under different case numbers in two groups involving different operations.

GROUP 1: EXPOSURE FOLLOWING TENOTOMY

CASE 1.—O. B., a man aged 61, showed left divergent squint of 50 degrees on the perimeter for near and for far vision. The right eye could be adducted 15 degrees and the left 20 degrees. The condition followed "cutting" of both internal rectus muscles at the age of 18 for convergent squint. The left internal rectus was found firmly attached to the sclera 11.5 mm. from the limbus in the midline. The attachment apparently involved only part of the muscle, since all the muscle which could be found made up a band only half the size of a normal internal rectus muscle. This band was separated from the sclera and advanced to a point 5.5 mm. from the limbus. A recession of 3.5 mm. was performed on the left

external rectus, which, although it had not been operated on, was inserted 8.5 mm. from the limbus. The motility of the left eye was much improved, but 20 degrees of divergence remained. The right internal rectus muscle was then exposed and found firmly attached 12.5 mm. from the limbus. It was advanced to 4.5 mm. from the limbus. The result was parallelism on the cover test for near and for far vision, with normal adduction of the left eye and 35 degrees of adduction of the right eye.

Case 2.—Mrs. M., aged 27, had been operated on by an advertising quack at the age of 12 for convergent squint. She was told that operation was performed on both eyes, but an operative scar was found only over the left internal rectus muscle. Left divergent squint of 50 degrees for near and of 60 degrees for distant vision (perimeter) was present, with left adduction of only 15 degrees past the midline. In abduction the left eye turned slightly up. At operation the left internal rectus muscle was found attached 11 mm. from the limbus and above the midline (fig. 1). Four millimeters of the muscle was resected and the

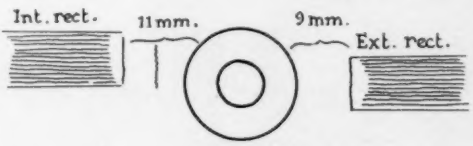

Fig. 1.—The condition in case 2 (left eye).

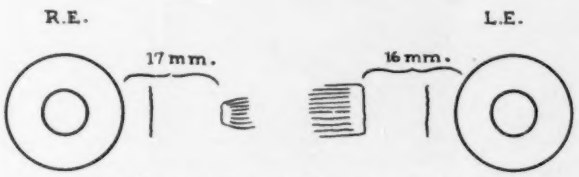

Fig. 2.—The condition in case 3.

cut end advanced to a point 3 mm. from the limbus. The muscle seemed normally elastic when separated from the sclera. A recession of 4 mm. was performed on the external rectus muscle, which was inserted 9 mm. from the limbus. The improvement in motility was marked, adduction becoming practically normal, but 10 degrees of divergence for distance and somewhat less than this for near vision remained.

Case 3.—G. G. a man aged 43, showed extreme divergent strabismus after a bilateral operation at the age of 16 by a well known traveling squint operator. This operator is known to have performed myotomies as a rule, and apparently the patient's operation was performed on both internal rectus muscles. Both eyes were turned far out, and neither could be brought to the midline. The angle of divergence was at least 60 degrees on the perimeter. At operation the left internal rectus muscle was found adherent to the sclera far behind the equator and about 16 mm. from the limbus. The muscle was short but when isolated from the sclera could be stretched to reach the limbus when the eye was rotated in (fig. 2). Two millimeters was resected, and the stump was sutured to the sclera 2 mm. from the limbus. A 5 mm. recession was performed on the external

rectus muscle. A month later the right internal rectus was exposed. It was difficult to be sure of the location of the muscle. Some fibrous tissue adherent to the sclera 17 mm. from the limbus was dissected free and was found to be attached to a rather inelastic band which seemed to contain some muscle fibers. The end of this band was attached to the sclera 2 mm. from the limbus. A recession of 6 mm. was performed on the internal rectus muscle. A great cosmetic improvement resulted (fig. 3). There is slight right divergence in the primary position. Adduction of the left eye is fairly good, but the right eye, in which isolation of the muscle was doubtful, can be brought only to the midline. This improvement has been maintained for six years.

CASE 4.—L. E., a man aged 44 (the same patient as in case 19), had tenotomies of the internal rectus muscles for bilateral abducens nerve paresis. Other operative procedures and their results are described in the report on case 19. On account of insufficient effect the left internal rectus muscle was exposed after two years. It was found adherent approximately to its old insertion. It was recessed 5 mm.

Fig. 3.—The result in case 3. *A*, primary position; *B*, eyes right; *C*, eyes left.

In the first 3 cases the well known tendency for the internal rectus muscle to slip back for an indefinite extent on the sclera after tenotomy and especially after myotomy is demonstrated. An interesting finding was the abnormal location of the insertion of the external rectus muscle in the first 2 cases, 8.5 and 9 mm. from the limbus. Was this originally present and hence a cause of the original convergent squint, or did adhesions occur behind the original insertion after myotomy of the opponent and as a result of contracture of the muscle? At any rate it demonstrates, as does a similar finding to be described in later cases, that an insertion of the external rectus muscle 8.5 to 9 mm. from the limbus does not prevent extreme divergent squint from developing and certainly does not interfere with abduction. In the fourth case, in which the tenotomized muscle was opposed only by a paretic external rectus muscle and transplanted slips from the vertical rectus muscles, attachment of the tenotomized muscle occurred practically at its old insertion.

On account of the hesitation of some surgeons to operate for divergence following tenotomy, it seems worth while to emphasize the fact that the muscle can nearly always be found and that when separated from its faulty insertion and replaced at or slightly in front of its normal insertion it acts as a living muscle capable of adducting the eye to a normal extent. This is true no matter how long it has remained in its faulty position. When divergence has existed for a long period, however, secondary contracture of the opposing muscle has occurred, requiring recession of that muscle, as a rule, in order to bring about parallelism. Similar results have been obtained in at least 3 cases on which the data at hand is not sufficient for inclusion in this paper. In no case has the secondary operation produced an overeffect with reestablishment of the type of squint originally present.

GROUP 2: EXPOSURE FOLLOWING RECESSION

In 3 of the cases in group 2 the original operation was for concomitant convergent squint, with resulting overeffect. In all these cases

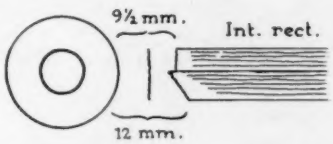

Fig. 4.—The operation in case 5 (right eye).

a combined operation was performed, comprising recession of the internal rectus muscle with advancement and resection of the external rectus. Lest this combined operation be condemned on the basis of the results reported, it may be stated that these, with case 12, are the only cases to be found in my files in which an overeffect sufficient to constitute a cosmetic defect was brought about by this combined procedure.

CASE 5.—Mrs. D., aged 30, showed right convergent squint of 15 degrees with right hypotropia of 7½ degrees on the perimeter. Since the convergence was the same for near and for distant vision it was decided to perform a small recession on the right internus muscle (3 mm.) with a small resection (4 mm.) and advancement (3 mm.) on the external rectus. At the same time an O'Connor cinch was performed on the right superior rectus. The result was a marked overeffect with exotropia of 24 prism diopters for distance and of 18 for near vision. Adduction was not greatly limited. No improvement having occurred in three months, the right internal rectus muscle was exposed. It was found divided into two bands which separated easily from each other. The upper band was 9.5 mm. from the limbus. The lower band was attached in an oblique line from 9 to 12 mm. from the limbus (fig. 4). Both bands were included in the advancement sutures and advanced by my technic to a scleral groove 4 mm. from the limbus. As a result the eyes showed no lateral deviation on cover test, though the Maddox rod test shows 4 to 8 degrees of exophoria for distance vision. There is still right

hypophoria of 8 to 12 degrees, which becomes a manifest hypotropia at times. At times a barely perceptible divergence for distant vision on cover test is seen.

CASE 6.—C. van P., a boy aged 14, showed alternating convergent squint of 30 prism diopters for distance and of 40 for near vision. The vision was below normal in each eye, and nystagmus was noted on even slight lateral movements. A 4 mm. recession was performed on the right internal rectus muscle and a 6 mm. resection with a 2.5 mm. advancement to a scleral groove on the right external rectus. A marked overeffect resulted, which decreased to 16 prism diopters during the next few months. Adduction was limited to 20 degrees, while abduction was excessive. Fusion was present, and exercises with the stereoscope were carried out. A year after the first operation the right internal rectus muscle was exposed. It was firmly attached 10.5 mm. from the limbus, or 5 mm. behind its original insertion (fig. 5). It was shortened by a 2 mm. resection and advanced to its old insertion. A year later there was still 10 prism diopters of divergence for distant vision, although parallelism at 16 inches (41 cm.) could be determined

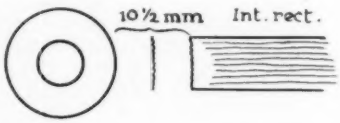

Fig. 5.—The operation in case 6 (right eye).

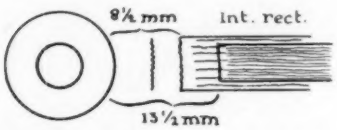

Fig. 6.—The operation in case 7 (right eye).

by an effort and adduction was much improved. An O'Connor cinch on the left internal rectus muscle produced parallelism for distant vision.

CASE 7.—N. S., a girl aged 5, showed convergent squint of 35 degrees with right sursumvergence of 10 degrees (perimeter). A recession of 3 mm. was performed on the right internal rectus muscle, with a 7 mm. resection and 3 mm. advancement of the right external rectus. A marked overeffect was noted at the first dressing, with almost complete absence of adduction. As this did not decrease, the internal rectus muscle was exposed eighteen days later. It was attached near its former insertion. A hook was swept beneath the muscle, but no abnormal adhesions were felt. Divergence of 15 degrees remained, and three months later the muscle was again exposed. The superficial layers of muscle were attached 8.5 mm. from the limbus, but a deep band of muscle was adherent to the sclera at least 5 mm. behind this point (fig. 6). This was separated, and the whole muscle was advanced to within 1.5 mm. from the limbus. Adduction was considerably improved, but considerable divergence remained. This was only slightly improved by a later recession of the advanced external rectus muscle. It was noted that upward movement of the right eye was limited to 10 degrees, which is difficult to explain unless one may assume that scar tissue had formed which held the eye in a relatively fixed position. There was nothing unusual about the reaction following any of the operations which would account for this limitation.

CASE 8.—M. V., a woman aged 22, was operated on for congenital paresis of the left abducens nerve. The outer halves of the superior and inferior rectus muscles were transplanted to the insertion of the external rectus, and a 5 mm. recession was performed on the internal rectus. The result was an overeffect, with 15 degrees of exotropia. The internal rectus muscle was exposed and found attached 11.5 mm. from the limbus, the attachment being of normal extent. It was separated from the sclera and advanced 9 mm. The result was good, with no deviation on cover test, adduction of 45 degrees and abduction of 20 degrees.

This case, with the exception of 1 other, which could not be followed, is the only one of 18 cases in which tendon transplantation with recession of the internal rectus muscle for abducens nerve paresis produced an overeffect. The overeffect in case 19, to be described, did not follow the original operation but followed a secondary procedure.

CASE 9.—Mrs. S., aged 32, had congenital paralysis of the left abducens nerve. She had been operated on three years before by an excellent surgeon, who furnished details of his procedure. A three stitch 4 mm. recession of the left internal rectus muscle and a 7 mm. Reese resection of the left external rectus had been performed. The eyes were straight for one year after this, and abduction of 15 degrees was obtained. When the patient was seen three years after operation, however, there was left convergence corrected by 35 degrees of prism. The left eye could be abducted 15 degrees. When the patient fixed with the left eye the right eye showed marked secondary deviation of 40 to 50 degrees, and it was this for which she sought relief. Both lateral rectus muscles were exposed. The internal rectus was found attached smoothly 11 mm. from the limbus. It was left undisturbed, and transplantation of the outer halves of the superior and inferior rectus muscles to a scleral groove 5 mm. from the outer limbus was performed. The condition of the external rectus is described in the report on case 14. The result five months after operation was satisfactory. No deviation was present in the primary position with the head straight, and binocular movement to the left of 20 degrees was possible without diplopia. The left eye alone could be abducted 30 degrees.[8]

CASE 10.—C. MacD., a man aged 42, had traumatic paralysis of the left superior rectus muscle, with enophthalmos, of two years' duration. There was diplopia in the whole upper field, and the left eye could be moved only 5 degrees above the midline. A recession of 5 mm. was performed on the left inferior rectus muscle, with a 4 mm. resection and 3 mm. advancement on the left superior rectus. The result was left hypertropia of 16 prism diopters, which remained the same during nine months. The left inferior rectus muscle was then exposed. It was found 12 mm. from the limbus, firmly attached to the sclera, and seemed short and inelastic. It was separated and advanced to a scleral groove 2 mm. from the limbus with a resection of 5 mm. This improved the motility of the eye, and, although the Maddox rod test still showed 12 D. of left hyperphoria, fusion was maintained over a binocular field extending 40 degrees above and 20 degrees below the midline, with 4 D. of vertical prism in the correction.

CASE 11.—J. M., a youth aged 20, showed a complicated combination of vertical and lateral deviation, probably the result of a partial paralysis of the right trochlear

8. Further notes on cases 3, 8, 9 and 19, in which tendon transplantation was performed, with illustrations in some cases, may be found in a previous article (Gifford, S. R.: Tendon Transplantation for Paralysis of the External Rectus Muscle, Arch. Ophth. **24**:916 [Nov.] 1940).

nerve. He had been operated on for the convergent factor a year before. There was still convergent squint, and the left internal rectus muscle was exposed. Apparently a recession had been performed. Most of the muscle was attached in a curved line near its old insertion 5.5 mm. from the limbus. At the lower edge of the muscle an adhesion to the sclera extended 2 to 3 mm. behind this attachment. The muscle was detached, and a recession of 4 mm. was performed, with fairly good correction of the convergence. The procedures to correct the vertical deviation need not be considered here.

CASE 12.—M. H., a girl aged 16, had been operated on previously for convergent squint, with insufficient effect. Recession of the left internal rectus muscle and resection and advancement of the left external rectus were followed after one year by a 5 mm. recession of the right internal rectus alone. Convergence of 20 prism diopters for distance and of 35 for near vision, with normal adduction, was still present a year later. The right internal rectus muscle was exposed, and a broad regular attachment was found. The attachment was 1.5 mm. wide as measured after it was separated from the sclera, the most posterior portion being only 6.5 mm. from the limbus. There were no adhesions back of this point. A recession of a further 3.5 mm. was performed with an O'Connor cinch on the external rectus muscle. The result was parallelism for distance, with 15 D. of convergence for near vision.

To summarize the findings in group 2, it may be said in general that these cases indicated a fairly great degree of accuracy in the location of the muscle after recession. In cases 6, 8, 9 and 10 the effective insertion of the muscle was within 1.5 mm. of the desired one as measured at the time of operation and there were no adhesions to the sclera back of this point. In the cases in which there was an overeffect, this could be explained as due to an overestimate of the desired surgical correction for the degree of squint present, usually with excessive shortening of the opponent. The exceptions were cases 5 and 7. In these cases separate bands of muscle were found adherent to the sclera behind the calculated insertion of the muscle, which interfered with adduction and accounted for the overeffect. These abnormal bands might be explained as due to failure of the operator to include all the muscle fibers in the sutures, slipping of a few fibers out of the forceps before the sutures were placed or formation of a clot with adhesion to the sclera of the fibers connected with it. In case 11 the type of operation was not known, or its extent, and it can be said only that the new insertion was close to the previous one, resulting in an insufficient effect. In case 12 the effective insertion was only 1 instead of the calculated 5 mm. from the original insertion. This is in accord with Dr. Davis' finding in several cases, muscle fibers in front of the sutures becoming adherent to the sclera. Apparently rotations of the eye following operation may in some cases free the muscle from the sclera at the site of the sutures, leaving the effective point of attachment at the site of the anterior adhesions. In case 12 the line of insertion was as firm and regular as if the muscle had been sutured in that position instead of 4 mm. posterior to it.

It will be noted that in the 2 cases in which the muscle attachment was found almost at its original site, no shortening operation had been performed on the opposing muscle. In the 2 cases in which abnormal adhesions were found *behind* the line of scleral sutures, shortening of the opponent had been performed. In a large number of cases shortening of the opponent was combined with recession. If one were to judge by the satisfactory effect of this combined procedure in most cases, it would be assumed that the permanent attachment of the recessed muscle was usually fairly near the line of sutures, although in none of the cases in which the result was satisfactory was the muscle exposed for examination. Certainly shortening of the opponent would tend to hold the eye in such a position as to prevent adhesions of the muscle *anterior* to the line of sutures.

GROUP 3: EXPOSURE FOLLOWING SHORTENING OPERATIONS

A. ADVANCEMENT AND RESECTION

CASE 13.—E. S., a boy aged 5, showed left convergent squint of 30 prism diopters for distance and of 40 for near vision. A 5 mm. recession was performed

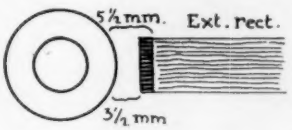

Fig. 7.—The operation in case 13 (left eye).

on the left internal rectus muscle and a 6 mm. resection with a 2 mm. advancement to a scleral groove on the left external rectus. A rather pronounced overeffect was apparent when the patient was on the operating table (general anesthesia), and this remained fairly constant after operation at about 15 prism diopters. Adduction was limited to 25 degrees, and abduction was excessive. Because of this excessive abduction and a desire not to further narrow the palpebral fissure, the left external rectus muscle was exposed three months after the first operation. It was found adherent over an area from the point of advancement to its old insertion 5.5 mm. from the limbus but perfectly free behind this point (fig. 7). It was separated from the sclera, and a recession of 4 mm. was performed. The cosmetic result was good, though very slight divergence for distance vision was still present on cover test. Adduction was restored to normal.

The finding in this case is in accord with Lancaster's belief that the advanced muscle always adheres to its original insertion and acts from this point.

B. REESE RESECTION

CASE 14.—The patient was the same one as in case 9. As previously stated, she had been operated on three years before, having had a Reese resection of 7 mm. on a paretic external rectus muscle. The muscle was found firmly adherent to the sclera 10 mm. from the limbus. No muscle fibers could be seen in front of this attachment. From the findings of Carroll and Blake it may be assumed that the

muscle fibers had become necrotic and that an adhesion, perhaps due to a blood clot, had formed behind the insertion to which the resected muscle was attached. This would have tended to nullify the effect of the resection and perhaps to limit motility, even if the muscle had not been paretic.

CASE 15.—M. M., a girl aged 11, had been operated on for convergent squint by a very capable colleague at the age of 4. A Reese resection (5 mm.) of the left external rectus muscle was combined with guarded tenotomy of the left internal rectus. When I saw the patient five years later there was left convergence with glasses corrected by 27 D. of prism base out for distance and 37 D. of prism for near vision. Without glasses 37 D. of prism for distance and 50 D. of prism for near vision was required. Motility was normal. At exposure of the muscle, the left internal rectus was found 3 mm. from the old insertion. It was set back 2 mm. farther. The external rectus was found to be 8 mm. from the limbus, or 2.5 mm. *back of its original insertion.* Five millimeters was resected, and it was advanced to a groove 3 mm. from the limbus. Two years later the eyes are parallel for near and for far vision with glasses. Without glasses there is slight convergence on cover test for near vision only. Motility is not disturbed as a result of the secondary procedure. The same explanation of the adhesion of the muscle *behind* its previous insertion would apply in this case as in case 14.

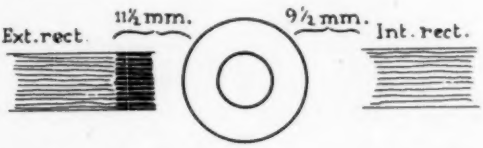

Fig. 8.—The operation is case 15 (right eye).

C. TUCKING

CASE 16.—J. K., a man aged 38, had been operated on by an excellent surgeon for convergent squint at the age of 25. This surgeon stated that only a tucking of the right external rectus muscle was performed. The squint was improved by this procedure, but when I saw the patient right convergence of 20 degrees on the perimeter and 30 degrees for near vision was present with correction. Both right lateral rectus muscles were exposed. The internal rectus, which was said never to have been operated on, was found attached 9.5 mm. from the limbus. The external rectus was attached 11.5 mm. from the limbus (fig. 8). The internal rectus muscle was not disturbed, but a 3 mm. resection was performed on the external rectus, and it was advanced to a scleral groove 3 mm. from the limbus. The result was parallelism for near and for far vision with glasses, while slight convergence without glasses remained.

As in the case of exposure following resection, it must be assumed that necrosis of the muscle occurred at the site of the tuck and that adhesion to the sclera developed far behind the original insertion. It is interesting that this occurred after a tuck in which the muscle fibers were not cut. The unusual location of the internal rectus muscle, which was apparently not operated on, is worthy of note. In spite of its abnormally posterior insertion the muscle was still able to produce a constant convergent deviation. A conjunctival scar over the muscle

suggested that an operation may have been performed in spite of the absence of any record of one.

GROUP 4: EXPOSURE FOLLOWING MYOTOMY OF THE INFERIOR OBLIQUE MUSCLE

CASE 17.—A. B., a boy aged 9, showed paralysis of the left superior oblique muscle with overaction of the left inferior oblique causing marked up-shoot of the left eye in adduction. The left inferior oblique muscle was exposed at its origin and cut loose from the periosteum, and the cut end was left free. The up-shoot of the left eye was absent for a month but recurred. Three months later the muscle was again exposed, and a thick band of muscle was found attached firmly near its original origin beneath the orbital margin. It was again cut loose from this attachment and freed carefully from attachment to the orbital fascia. Four millimeters of the muscle was resected. At the same time a 5 mm. recession of the right inferior rectus muscle was performed. The result was a reduction in the left hypertropia from 20 to 8 prism diopters and absence of the up-shoot on adduction. The condition had further improved four years after the second operation.

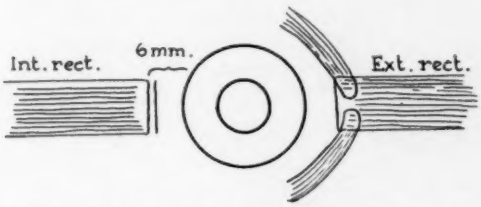

Fig. 9.—The operation in case 19 (left eye).

CASE 18.—Mrs. W., aged 65, showed complete paralysis of the left superior rectus muscle following exophthalmic goiter. Other muscles had been involved, but practically complete function had returned to all except this muscle. Advancement of the paretic muscle was followed later by myotomy of the right inferior oblique with a resection of 4 mm. This reduced the left hypertropia for six months, but it then became as bad as before, while the motion of the right eye up and in, which was at first limited, became practically normal. Eighteen months after the first myotomy, the right inferior oblique muscle was exposed. It was difficult to find the muscle at its origin. A good deal of connective tissue was severed near the original origin, and a few muscle fibers were found attached somewhat back of the orbital margin. These were also cut, but this procedure had little effect on the motility of the eye, which could still be moved up and in to a practically normal extent. In explanation of this motility after two complete sections of the muscle it must be assumed either that an abnormally deep secondary origin was present, which could not be found, or that adhesions of the muscle to the orbital fascia allowed it to act from a fixed point in the orbit in a practically normal manner.

GROUP 5: EXPOSURE FOLLOWING TENDON TRANSPLANTATION FOR ABDUCENS NERVE PARALYSIS

CASE 19.—L. E., the same patient as in case 4, had bilateral abducens nerve paralysis following skull fracture. On account of extreme contracture of both internal rectus muscles tenotomies were performed on these muscles and bilateral transplantation of the outer halves of the superior and inferior rectus muscles beneath the insertion of the external rectus muscles. Marked cosmetic and functional improvement resulted, but owing to some remaining convergence the left internal and external rectus muscles were exposed two years later. The condition of the internal rectus has been described in the report on case 4. Exposure of the external rectus showed the slips from the superior and inferior rectus muscles in place beneath the insertion. They crossed the sclera fairly far back to reach this location and were not adherent to the sclera at any point except the insertion (fig. 9). The paretic muscle was advanced almost to the limbus, the internal rectus was recessed 5 mm. and the eye was held in an abducted position by a tension suture. The result was a considerable improvement in the cosmetic effect, 15 degrees of left convergence remaining.

CASE 20.—B. L., a girl aged 12, had a tendon transplantation and recession of the internal rectus muscle on the left eye for congenital abducens nerve paralysis.

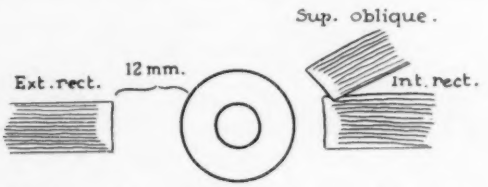

Fig. 10.—The operation in case 20 (right eye).

The effect was insufficient, and the internal and external rectus muscles were later exposed. The internal rectus was found adherent near its old insertion and was tenotomized. The transplanted muscle slips from the superior and inferior rectus muscles were attached firmly beneath the insertion of the external rectus, having formed shallow lines of depression in the sclera but without adhesion to the sclera. The paretic muscle was advanced 2 mm., and 5 mm. was resected. The immediate result was a slight overeffect, with some limitation of adduction, but the patient was not followed long after the operation.

In these 2 cases it seems of interest to have proved by exposure that the tendon slips actually remain attached firmly in their new location and that adhesions to the sclera elsewhere do not occur.

GROUP 6: EXPOSURE FOLLOWING TRANSPLANTATION OF THE SUPERIOR OBLIQUE MUSCLE

CASE 21.—L. W., a woman aged 41, had extreme divergence of the right eye resulting from oculomotor nerve paralysis. The ptosis had cleared up, but the right eye was held in extreme abduction and could not be moved nearer than 35 degrees from the midline. Wiener's procedure was performed, the right superior oblique muscle being separated from the pulley, cut in front of its insertion on the globe, 1.5 cm. of it resected and the stump sutured to the sclera 2.5 mm. in

front of the insertion of the internal rectus. There was some improvement, but the right eye was still above the left. At a third operation the transplanted muscle was exposed. It was found firmly adherent to the sclera slightly above the insertion of the internal rectus muscle (fig. 10). It was freed from a rather broad attachment and from fascial attachments as far back in the orbit as possible. Five millimeters was resected, and it was sutured carefully in a scleral groove 2 mm. in front of the insertion of the internal rectus muscle. This procedure improved the position of the eye considerably. It was only slightly sursumvergent, and the primary divergence was reduced from a previous 70 degrees to 30 degrees. The eye could be moved to the midline but not past it when the patient looked to the left.

GROUP 7: EXPOSURE OF MUSCLE TO RELIEVE DIPLOPIA FOLLOWING OPERATION FOR RETINAL DETACHMENT

CASE 22.—W. G., a man aged 66, was operated on for retinal detachment of three months' duration. The external rectus muscle was tenotomized and replaced at its insertion with two sutures. Coagulation was from 9 to 17 mm. back of the limbus in the region beneath the muscle and resulted in healing of the detachment. Divergence of 40 prism diopters followed the operation, and four months later the muscles were exposed. The external rectus was found firmly attached 10.5 mm. from the limbus. No muscle fibers could be seen in front of this attachment. The muscle was not disturbed, but a 6 mm. resection and 3 mm. advancement was performed on the internal rectus muscle. The result was 9 prism diopters of exophoria and 3 of left hypophoria, which were corrected by prisms in the glasses.

CASE 23.—R. M., a youth aged 18, was operated on for retinal detachment of two years' duration resulting from a traumatic macular hole. Right divergence was present before the operation; so instead of the external rectus muscle's being replaced at its insertion, it was sutured to the sclera 5 mm. behind its insertion. Perforating coagulation was chiefly in the macular region with flat coagulation below, nothing being done near the insertion of the external rectus muscle. The retina healed flat after operation, but central vision was not improved, as was expected from the scars produced in the macular region. The divergence was not improved by recession of the external rectus muscle and continued to increase, measuring 40 degrees on the perimeter after one year. The external rectus was exposed and was found to have a broad attachment extending from 9 to 12 mm. from the limbus. A safety suture was placed through the muscle and was tied loosely. The internal rectus was resected 6 mm. and advanced 2 mm. The cosmetic result was good.

CASE 24.—Mr. B., aged 39, had two operations for retinal detachment. A small localized area of detachment was left, but the retina was fixed by scars and the holes were closed. Vision was 20/200. At the first operation the inferior rectus muscle was tenotomized and replaced with two sutures to its insertion. Coagulation included most of the lower half, extending beneath the location of the muscle. There was no vertical deviation after this operation, but at the first dressing a divergence was noted. At the second operation the inferior rectus muscle was found fixed in a mass of scar tissue and adherent to the sclera for 3 to 4 mm. back of its insertion. It was dissected from the sclera and replaced at its previous insertion. The divergence remained approxmiately 30 degrees on the perimeter. One year after the second operation the internal and external rectus muscles were

exposed. The internal was adherent to the sclera back to 8.5 mm. and the external back to 11 mm. from the limbus. These muscles had not been operated on previously, but the coagulation, while not extending under the muscles, was fairly close to them and especially close to the external rectus. It must be held responsible for the adhesions formed. The external rectus muscle was freed and a safety suture placed through it and tied loosely. The internal rectus was resected 4 mm. and advanced to 3 mm. from the limbus. After five months slight divergence for distance vision on cover test was present, but the cosmetic result was satisfactory.

In this group of cases the abnormal adhesion of the muscle to the sclera must be ascribed to the reaction following coagulation. This was true in case 24 of muscles which had not been tenotomized. The remarkable fact is that in spite of the adhesions, divergence developed in all cases, which was overcome only by shortening and advancing the internal rectus muscle. In case 23 divergence increased in spite of recession of the external rectus at the first operation.

COMMENT AND CONCLUSIONS

1. The findings in group 1 only add to previous evidence indicating the danger of free tenotomy in convergent squint.

Great improvement may be obtained in such cases even after many years by isolating the tenotomized muscle and replacing it at or slightly in front of its previous insertion. When contracture of the external rectus muscle is severe it is necessary to perform recession on this muscle.

2. Recession produced in most cases a new insertion at or very close to the location of the scleral sutures.

In 2 cases bands of muscle became adherent behind this point, resulting in overeffect and limitation of adduction. In both cases shortening of the external rectus muscle had been done. Care in placing forceps and sutures and careful hemostasis should make this complication a rare one. In 1 case and possibly a second, muscle fibers became adherent or grew forward in front of the scleral sutures, resulting in an insufficient effect. In neither case had shortening of the opponent been performed.

3. After Reese resection and tucking, adhesions were found far back of the original insertion, which nullified the effect of the operation. This may be explained, according to Carroll and Blake's experimental findings, as due to necrosis of muscle fibers or to clot formation with resulting adhesion of the muscle at the point which is not necrotic. In the only case of resection and advancement available, adhesion occurred to the previous insertion but not behind it. If any conclusion were to be drawn from this, it would be that resection plus advancement to a scleral groove gives a firm and broad insertion which is perhaps not so apt to extend back of the original insertion as after resection alone or tucking.

in which fibers are traumatized in a location where they may easily become adherent to the sclera.

4. After myotomy of the inferior oblique muscle, as is well known, the muscle may become reattached near its origin. To prevent this it is advisable to resect 4 mm. of the muscle and to free it completely from fascial attachments.

5. In 2 cases of tendon transplantation for abducens nerve paralysis the tendon slips were found in good position inserted firmly beneath the external rectus muscle.

6. After Wiener's procedure the superior oblique muscle may slip back of its sutured position and above this point. It must be freed from fascia far back in the orbit and made to pass horizontally toward its new insertion to avoid elevation of the eye. The advantage of care in this respect was shown in a recent case not included here.

7. Coagulation for retinal detachment may cause adhesions of muscles to the sclera, whether or not these have been resected. Such adhesions do not prevent deviation of the eye in the direction of the adherent muscle when a tendency to divergence is present.

8. Insertions abnormally far from the limbus were found in the case of several muscles not previously operated on.

A VISUAL TEST CARD DESIGNED FOR USE IN EXAMINATIONS FOR THE ARMED FORCES

A MORE REFINED MEANS FOR DIFFERENTIATING BETWEEN CLASS 1-A AND CLASS 1-B REGISTRANTS

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The purpose of this paper is to present a visual test card that has been adapted to the needs of the examination for entrance into the armed forces. This examination presents certain problems that are not usually encountered in the routine examination of eyes in private practice. Now, at a time when the armed forces are being rapidly expanded, large numbers of men are examined in groups and the measurement of vision must be accomplished quickly and as accurately as possible as part of the whole examination. Every effort must be made to determine the man's true vision during this hurried examination, as the examiner is confronted both by men with poor vision, who are anxious to get into the service and so try to make their vision appear better than it actually is, and by men who are malingering to evade service. The test conditions and the tests used should be simple and yet give some check on the visual acuity obtained. The test of visual acuity is only a small portion of the examination given each man and may be taken lightly, but it assumes greater importance when one considers the number of men rejected for general military service because of defective vision alone.

A preliminary report by Colonel Leonard G. Rowntree, chief of the Medical Division of the Selective Service System, dated Oct. 2, 1941,[1] gives ocular abnormalities as the second major cause for disqualification, accounting for 13.7 per cent of the total disqualifications. Statistical information compiled from the draft records after the last war and prepared under the direction of the Surgeon General's Office [2] shows that among the 2,753,922 men considered in that study defective vision

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The necessary tests on which this paper is based were made at the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

1. Release No. 236, National Headquarters, Selective Service System, Washington, D. C., Oct. 2, 1941.

2. Love, A. G., and Davenport, C. B.: Defects Found in Drafted Men. Washington, D. C., Government Printing Office, 1920.

and blindness comprised the third largest group of defects. Defective vision was found in nearly three per one hundred men examined.

The visual test card and the method of examination described hereafter are offered as an aid in reducing to a minimum rejections due to defective vision. The accurate measurement of sight is subject to psychic and physical variabilities, many of which cannot possibly be controlled. This paper deals with those factors that may be easily controlled—the visual test objects and the conditions under which the examination is conducted.

Letters and numerals are now used fairly uniformly as the test objects in examinations of visual acuity. However, it is well known that letters vary widely in their legibility. The American Medical Association's committee on standardizing test cards for visual acuity in its report in 1916 [3] gave a comparison of the relative legibility of the letters commonly used for testing visual acuity. The committee found that on comparing the eighteen letters chosen, with the letter "B" as a standard, the visual acuity required for the recognition of the other letters was somewhat less, as follows:

L	.71	D	.82
T	.74	Z	.84
V	.78	N	.85
U	.79	E	.85
C	.79	R	.88
O	.80	S	.89
Y	.80	G	.92
F	.81	H	.92
P	.81	B	1.00

This comparison also showed that two persons with full visual acuity and fully corrected ametropia differ slightly with respect to the order of visibility of some of these letters. Therefore, the list represents the averages obtained. While the committee reported that it was impossible to establish a scale of letters by which the visual acuity of different persons can be measured with anything like mathematical exactness, they said that the eighteen letters selected are about the best that can be chosen from the English alphabet both for scientific exactness and for practical usefulness. They then suggested that these letters be divided into the following four groups, each successive group containing letters more difficult to recognize.

L	T	V	U	C
O	Y	F	P	D
Z	N	E	R	
S	G	H	B	

3. Report of Committee on Standardizing Test Cards for Visual Acuity, Tr. Sect. Ophth., A. M. A., 1916, pp. 383-388.

They suggested further that each line of the test card should contain at least one letter from each group. A number of the cards now used do not conform to these recommendations.

Landolt's optotypes (a series of black rings on a white ground, each ring broken at one part for a space equivalent to the width of the black ring) avoid this difference in legibility of the letters and numerals but present definite drawbacks as a practical means for the examination of large groups of men for the armed forces. They may be used as an additional test in some doubtful cases as well as in testing the vision of illiterates.

In addition to the type of test card used, it is important to consider the illumination of the test chart and of the examining room. Visual acuity increases with the illumination of the test cards up to an intensity level of 15 to 20 foot candles.[4] Here the acuity curve changes its slope suddenly, and beyond 50 foot candles there is only a slight rise. The general illumination level of the test room should not be less than one tenth of that of the test chart; one fourth is preferable, and some experimentors have specified equality. Cobb [5] reported that the speed of vision shows a maximum at about 40 foot candles.

Some of the test cards in use have colored lines or numerals at different levels on the chart. Individual examiners frequently mark or underscore certain lines to call attention to them in an effort to speed up the examination. These identifying marks make it easier for word to be circulated among the group undergoing examination as to how much each one is expected to read.

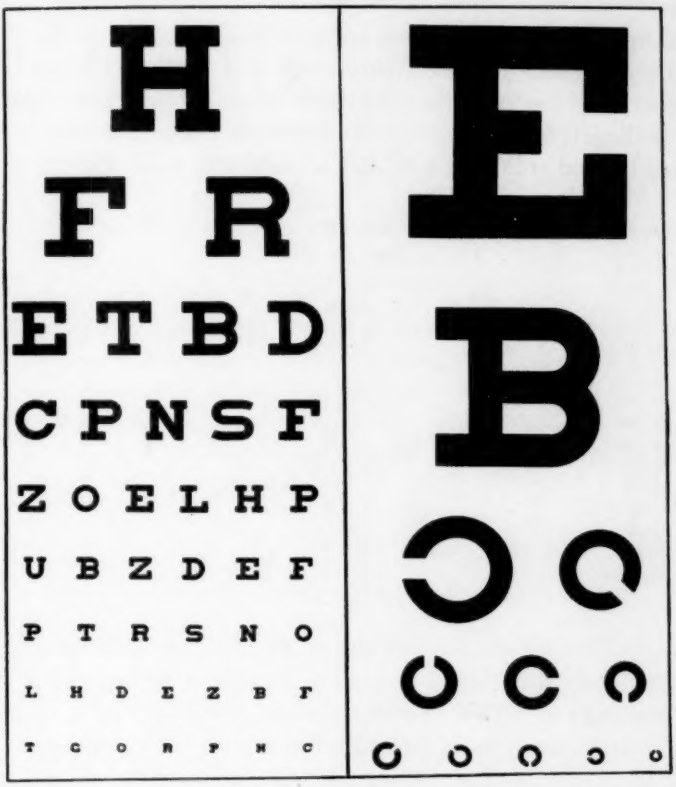
The test cards in general use almost without exception have one 20/200 letter at the top and immediately beneath it two 20/100 letters. These three letters represent the dividing line between general and limited military service as far as uncorrected vision is concerned. Frequently the two letters on the 20/100 line vary so widely in their legibility that one of the letters is read correctly while the other is missed. This presents a problem as to the proper classification. Few of the test cards in use have a 20/400 letter.

The test chart that is herein presented has been constructed to meet some of the problems noted. The letters have been selected from those recommended by the committee of the American Medical Association as

4. Hardy, L. H.: The Measurement of Sight, Tr. Illumin. Engin. Soc. **35**: 619, 1940.

5. Cobb, P. W.: Some Experiments on the Speed of Vision, Tr. Illumin. Engin. Soc. **19**:150-178, 1924. Cobb, P. W., and Moss, F. K.: Four Fundamental Factors in Vision, ibid. **23**:469-506, 1928. Cobb, P. W.: The Relation Between Field Brightness and the Speed of Retinal Impression, J. Exper. Psychol. **8**:77-108, 1925.

well as from those agreed on by the authorities quoted by Cowan [6] in his excellent review of the subject. These letters were drawn to conform to Snellen's test types. On one side of the card the top single letter represents 20/200 vision and the next two letters 20/150; the second line has been added to bridge the jump from 20/200 to 20/100. As 20/100 vision is the lower limit of vision in the present standards for



The visual test card presented.

acceptance for general military service, the number of letters on this line has been increased from two to four. The next line is 20/75 instead of 20/70 because when read at 15 feet (457 cm.) the vision is equivalent to 20/100 for all practical purposes. The remaining lines are 20/50, 20/40, 20/30, 20/20 and 20/15, the same as those found on most test charts. The letters on these smaller lines have been separated more

6. Cowan, A.: Test Cards for the Determination of the Visual Acuity: A Review, Arch. Ophth. **57**:283-297, 1928.

than usual to avoid any confusion that might result from the crowding of letters in the center of the line.

The reverse side of this card presents a 20/400 and a 20/300 letter. There is also a series of Landolt's "broken rings" as follows: one 20/200, one 20/150, two 20/100, one 20/75, one 20/50, two 20/40, one 20/30 and one 20/20. These may be used when desired as a check of the vision obtained with the letters or for testing illiterates. There are no notations beside the letters to indicate the vision each represents.

It is recommended that when vision is tested with this card the vision of each eye be tested at a distance of 20 feet (610 cm.) from the card and again at 15 feet from the card if the vision is below acceptable limits. Many malingerers after several examinations know how much they are expected to read at 20 feet but have no idea how much they should read

Approximate Equivalents of Vision for Distances of 20, 15 and 10 Feet from the Chart

For Vision Obtained at 20 Ft.	Corresponding Vision at 15 Ft.	Corresponding Vision at 10 Ft.
20/400	15/300	10/200
20/300	.....	10/150
20/200	15/150	10/100
20/150	.....	10/75
20/100	15/75	10/50
20/75	.....	.....
20/50	.....	.....
20/40	15/30	10/20
20/30	.....	10/15
20/20	15/15	.....
20/15	.....	.....

at 15 or 10 feet (305 cm.). The size of the letters is such that there is a line on the chart that should be read at 15 and at 10 feet corresponding to the line read at 20 feet for the various levels of vision that are of particular importance in examination for service with the armed forces.

The accompanying table shows the line that should be read at 15 and at 10 feet corresponding to the line read at 20 feet. These distances should be accurately measured from the chart and not estimated by the examiner. The examining room should be well illuminated without great contrast between the general illumination and the illumination of the test card. The test card should receive at least 20 foot candles of illumination uniformly distributed. The figures given, while not exact equivalents, will be found to correspond very well when the person examined reads just as much as he can at each distance. When the person is malingering or when he "squints" at one distance and not at another, a wide discrepancy will be noted. This should attract the examiner's attention and lead to further tests for malingering.

Even though there is approximately ⅓ D. of accommodation required at 10 feet, the slight help given a myopic subject and the slight burden added to the hyperopic present no serious objection if the 10 foot test is used only as an added check to rule out malingerers. There can be less objection to the testing of vision at 15 feet, and certainly the additional evidence obtained by a second measurement of the vision from this distance would be of great value in determining the proper classification of any candidate for the armed forces. Those persons who have extremely poor vision due to large refractive errors or to organic disease of the eyes and also those who read 20/20 test type at 20 feet offer no problem. However, this chart with the method of examination outlined has been shown to be of value in more clearly differentiating the borderline cases, as well as in pointing out the malingerers.

SUMMARY

A visual test card has been designed to meet the special requirements of examinations for the armed forces. Particular emphasis has been given those levels of vision that divide the men examined into the various classes as far as vision is concerned. Through the use of this card by the method suggested, a simple check of vision is obtained and attention is called to many malingerers. It has been found that this method of examination is of value in determining the classification of borderline cases.

THE CORNEA

I. TRANSFER OF WATER AND SODIUM CHLORIDE BY OSMOSIS AND DIFFUSION THROUGH THE EXCISED CORNEA

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The cornea is especially suitable for the study of permeability in biologic membranes not only because of its continued functional integrity after the death of the animal but because its anterior layer (epithelium) and posterior layer (endothelium and Descemet's membrane) may be separately removed without appreciable damage to the adjacent substantia propria. By comparing variations in permeability before and after removal of these membranes, it is theoretically possible to allocate the functional characteristics of the permeability to the different layers of the cornea.

Nevertheless, recent studies of corneal permeability have been few and have led to conclusions that are mutually contradictory.[1] Gallenga (1927)[2] found that salicylates, sulfocyanides and iodine placed on the cornea of the intact eye were subsequently detectable in the aqueous and that, at least in the case of iodine, hypertonic solutions on the outside of the eye caused water to pass through the cornea. From his qualitative tests he concluded that the cornea is not a semipermeable membrane.

Fischer (1928),[3] employing a small collecting chamber filled with concentrated sugar solution on the anterior surface of the cornea, found only traces of chloride in the vessel after two hours and believed that these came out of the cornea itself rather than from the aqueous. Water, on the other hand, was almost completely withdrawn from the anterior chamber in the process.

To study the transfer of chloride in the reverse direction, Fischer irrigated the anterior surface of the living eye with 5 per cent solution

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1. The older literature on corneal permeability has been reviewed by Leber, in Graefe, A., and Saemisch, E. T.: Handbuch der gesammten Augenheilkunde, Leipzig, W. Engelmann, 1903, vol. 2, pt. 2, chap. 11, p. 355.

2. Gallenga, R.: Influenza della pressione osmotica sull'assorbimento delle soluzione medicamentose attraverso la cornea, Arch. di sc. biol. **9**:212-223, 1927.

3. Fischer, F. P.: Untersuchungen über Quellungsvorgänge und über Permeabilitätsverhältnisse der Hornhaut, Arch. f. Augenh. **98**:41-65, 1928.

of sodium chloride and found the salt content of the aqueous increased from an average of 0.708 to 0.798 per cent (in the dead eye it was considerably greater), while with the epithelium removed the sodium chloride content rose to an average of 1.522 per cent. Removal of the endothelium and subsequent irrigation caused a rise to 0.885 per cent. Fischer concluded that the cornea is unidirectionally permeable to sodium chloride, i. e. in the direction out-in, with the epithelium and the endothelium forming the limiting barriers. According to this author, therefore, the cornea possesses the same permeability characteristics as had previously been shown for frog's skin by Wertheimer.

Ridley (1930),[4] using other salts, came to quite different conclusions. The most pertinent of Ridley's experiments were those in which he placed 1 per cent solution of ammonium chloride or potassium sulfocyanate on either side of the cornea and detected ammonia or sulfocyanate on the other side irrespective of the orientation of the cornea. This led the author to conclude that the cornea is permeable to salts in both directions. The removal of epithelium in the experiments produced a slight increase in permeability. The actual barrier to the free transfer of fluid through the cornea, according to Ridley, was Descemet's membrane because incision of this membrane caused the local clearing of a cornea stained with methylene blue.

Klein and Sárkány (1938) [5] also presented data on the permeability of the cornea to salt and water. They placed the excised cornea between Ringer's solution and blood to which had been added various amounts of Ringer's solution. The volume changes on each side were recorded in capillary tubes; in no case were they found to be greater than 0.02 cc. These authors' data are difficult to interpret, since the volume changes on the two sides did not counterbalance each other. It would seem likely that the small changes they found were attributable to variations in temperature or to turgescence rather than to transfer of fluid. However, they interpreted their results as indicating that the cornea is permeable to salt and water in both directions.

Iwai (1938) [6] studied the permeability of excised layers of cornea to potassium chloride, ascorbic acid, crysoidine crystal, neutral red, potassium fluoresceinate and water blue. His conclusions, which are all

4. Ridley, F.: An Experimental Investigation into the Intraocular Pressure and Drainage of the Aqueous Humour: I, Tr. Ophth. Soc. U. Kingdom **50**:268-309, 1930.

5. Klein, M., and Sárkány, J.: Experimental Data on the Problem of the Permeability of the Cornea: II. The Permeability of the Excised Cornea with Respect to Water and Chloride Ions, Brit. J. Ophth. **22**:409-417, 1938.

6. Iwai, M.: Das Verhalten der einzelnen Hornhautzellschichten für Permeabilität, Acta Soc. ophth. jap. **42** (pt. 2):101, 1938.

that were available to us, are that the epithelium, Bowman's membrane and Descemet's membrane are unidirectionally permeable in the out-in direction; that endothelium is unidirectionally permeable in the in-out direction and that the substantia propria is permeable equally in both directions.

The experiments here to be reported pertain to the transfer of water and sodium chloride through the cornea. The following technic was employed throughout:

Cat corneas were excised and securely tied on to the flared ends of 5 cc. graduated pipets, the tapered ends having previously been removed. The area of corneal surface exposed to the lumen of the tube approximated 385 sq. mm. The tubes, which were supported on individual ring stands, were partly filled with one fluid, and the ends holding the corneas were immersed in flasks containing a second fluid (fig. 1). Transfer of water was indicated by changes of the level

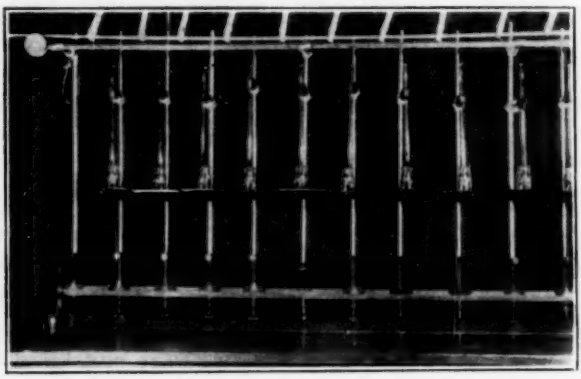

Fig. 1.—Partial view of the apparatus used for osmosis and diffusion experiments.

of fluid in the tube, while transfer of sodium chloride was indicated by variations in the chloride content of the fluid in the flask. The chloride determinations were made according to Fajans'[7] method.

Concentration gradients in the tubes were avoided by employment of the following apparatus to create continuous stirring: Small brass weights were suspended by clock wire to an overhead shaft. The shaft was connected to an eccentric from a motor which caused it to oscillate twenty times per minute, alternately raising and lowering the weights in the tubes.

Measurements were made on whole corneas and on corneas from which the following layers had been removed: epithelium, endothelium and Descemet's membrane and a combination of these layers which left

7. Fajans, K.: Oberflächenkräfte bei heteropolären Kristallgittern. Adsorption von Bleiisotopen an kolloidalen Silverhalogeniden, Ztschr. f. physik. Chem. **97**: 478-502, 1921.

only substantia propria. Unfortunately, as Leber [8] previously observed, it was impossible to obtain whole corneas without some damage to the endothelium. This damage probably occurred in the process of handling, but it did not involve Descemet's membrane. Therefore any effect which was observed after removal of both the endothelium and Descemet's membrane must be attributed wholly or in part to Descemet's membrane, and all the effects observed for the whole cornea (or cornea from which the epithelium had been removed) must be interpreted in the light of partial endothelial damage. Complete removal of the endothelium and Descemet's membrane was accomplished after excision of the cornea by scraping off the posterior surface with a knife. Histologic sections of several corneas so treated showed this to be satisfactorily accomplished. Removal of the epithelium was performed before excision of the cornea by scraping the anterior corneal surface with a cataract knife and following the denuded zone in light specularly reflected from a window.

In determining the net amount of water transferred as a result of osmosis, 4 cc. of distilled water was placed in the tube and 100 cc. of 5 per cent sodium chloride solution in the flask. A correction was made by subtracting a blank for the small loss of water due to evaporation. No attempt was made to buffer the solutions, as it has been shown [9] that the introduction of other ions sometimes greatly alters the transfer of the test ion. Instead the solutions were allowed to assume the p_H determined by the buffering capacity of the cornea. The p_H of the solutions in the tubes and flasks was measured electrometrically at the conclusion of each experiment and in a series of controls at various stages during the experiment. In all cases the p_H attained a value of 6.5 ± 0.2 within a few minutes and remained approximately constant.

Figure 2 represents the water transferred through the cornea (average of eight determinations for each curve) under the conditions set forth. The maximum variation at the end of the fourteen hundred minutes was less than 0.5 cc. It may be seen from the figure that water passed through the cornea when the epithelium was present and did so at a rate that was practically constant for the twenty-four hours of the experiment. This occurred only in the anterior direction and then only for the whole cornea (A) and for the cornea from which the endothelium and Descemet's membrane had been removed (B). Apparently removal of the endothelium and Descemet's membrane facilitated the transfer of water to a small extent. The transfer of water in the reverse direction could not be ascertained with the epithelium in situ because bullae formed

8. Leber, T.: Studien über den Flüssigkeitswechsel im Auge, Arch. f. Ophth. (pt. 2) **19**:87-186, 1873.

9. Michaelis, L., and Perlzweig, W. A.: Studies on Permeability of Membranes: I. Introduction and the Diffusion of Ions Across the Dried Collodion Membranes, J. Gen. Physiol. **10**:575-598, 1927.

whenever the solution on the anterior surface was hypotonic to that on the posterior surface. As will be described later, this resulted in a complete separation of the epithelium from the substantia propria.

Preliminary removal of the epithelium or a combination of epithelium, endothelium and Descemet's membrane resulted in a negligible volume change during the same test period under otherwise identical conditions.

The transfer of water by diffusion through the cornea in the absence of any osmotic force was investigated by making use of the fact that heavy water (a mixture of deuterium hydroxide and oxide) has a diffusion rate practically identical with that for ordinary water [10] and yet may be differentiated from it by virtue of its higher specific gravity. The technic previously employed was modified as follows:

A known concentration of heavy water was used in making 1 per cent sodium chloride solution, and 3.5 cc. of this liquid was placed in each of eight flasks;

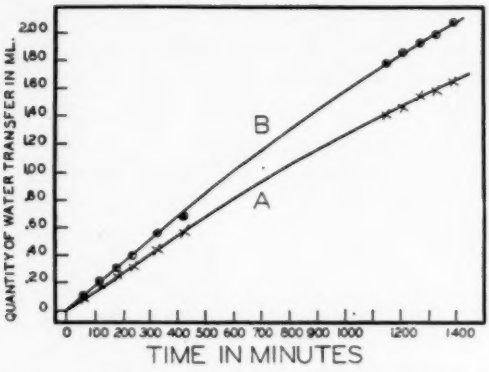

Fig. 2.—Average quantity (eight determinations for each curve) of water transferred through the cornea in a posterior to anterior direction by osmotic pressure (initially, 5 per cent sodium chloride solution). *A*, cornea intact; *B*, the endothelium and Descemet's membrane removed. (No net water change was demonstrable in an anterior to posterior direction or in either direction in the absence of epithelium; see text.)

2 cc. of 1 per cent sodium chloride solution made up in ordinary water was placed in each of the corresponding tubes. The fluid in the flasks was overlaid with sufficient paraffin oil to eliminate any hydrostatic pressure and incidentally to prevent evaporation. The corneas were studied in pairs, so that when the effect of the epithelium on water transfer was to be determined, one of the paired eyes was whole and the other was without the epithelial layer. All corneas were fastened on the tubes with the outer surface upward. The stirring of the fluid in the tubes was accomplished as in the former experiments. In addition, the fluid in the flasks was stirred at half hour intervals by thorough shaking. The experiments were carried out at room temperature, which was about 23 C.

10. Hevesy, G. E.: Der schwere Wasserstoff in der Biologie, Naturwissenschaften **23**:775, 1935.

At various intervals samples of the tube fluid were taken and the amount of heavy water that had diffused through the cornea was calculated from the increase in specific gravity of the fluid. To ascertain the latter a constant gradient tube was prepared and used according to the technic devised by Linderstrøm-Lang.[11] Since the chance that an ordinary water molecule will diffuse through the cornea is practically identical with the chance that a molecule of heavy water will, it follows that if the quantity of heavy water which has been transferred in a unit time and the proportion of heavy water present are known, the total water movement per unit time (rate) may be readily calculated. Such a calculation has been performed for the preceding experiments, and the rate so obtained is plotted as a function of time in figure 3. Each curve represents the average of 4 separate experiments.

It is apparent from curve *A* that considerable water diffused through the whole cornea and that the removal of the epithelium (curve *B*)

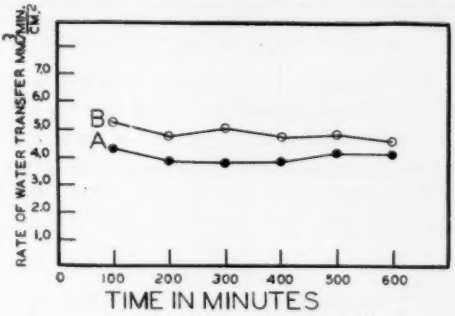

Fig. 3.—Average rate (four determinations for each curve) of water transferred through the cornea by diffusion (23 C.). *A*, cornea intact; *B*, epithelium removed.

enhanced the rate about one fifth. It should be emphasized that since there is no force resulting from osmosis or hydrostatic pressure no volume change occurs throughout the process; water simply goes back and forth.

For the study of sodium chloride transfer through the cornea, 2 cc. of 5 per cent sodium chloride solution was placed in each tube and the corneal ends were immersed in individual flasks containing 10 cc. of distilled water. At specified intervals the fluid in the flasks was removed for chloride analyses. A correction was made for sodium chloride contamination arising from the cornea itself by subtracting from all first analysis values 1.8 mg., the average amount found in water controls. As the passage of sodium chloride through the cornea resulted in a

11. Linderstrøm-Lang, K.; Jacobsen, O., and Johansen, G.: Measurement of the Deuterium Content in Mixtures of H_2O and D_2O, Compt. rend. d. trav. du Lab. Carlsberg, série chim. **5**:17-25, 1938.

decrease in the amount of this material available to go through the membrane, the rate of sodium chloride transfer is calculated on the basis of a constant amount of sodium chloride in the tube, i. e. 50 mg. per cubic centimeter. This is then plotted in the accompanying graphs as a function of time. Figure 4 represents the transfer in the posterior-anterior

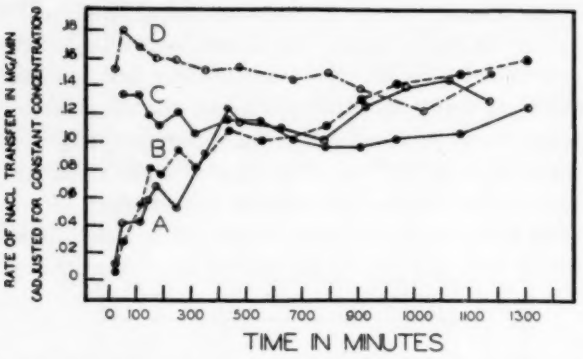

Fig. 4.—Average rate (seven to ten determinations for each curve) of sodium chloride transferred through the cornea in a posterior to anterior direction by diffusion, corrected so that a concentration gradient of 50 mg. per cubic centimeter was maintained constant throughout the experiment. *A*, cornea intact; *B*, endothelium and Descemet's membrane removed; *C*, epithelium removed, and *D*, epithelium, endothelium and Descemet's membrane removed.

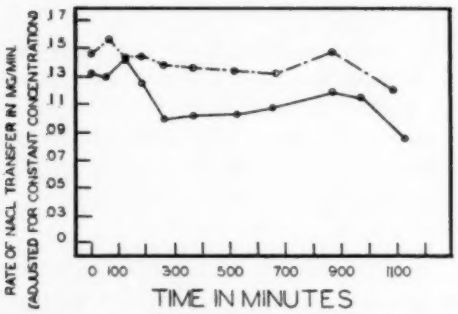

Fig. 5.—Average rate (eight determinations for each curve) of sodium chloride transferred through the cornea in an anterior to posterior direction by diffusion, corrected so that a concentration gradient of 50 mg. per hundred cubic centimeters was maintained constant throughout the experiment. Continuous line, epithelium removed; broken line, epithelium, endothelium and Descemet's membrane removed. (No sodium chloride was transferred in this direction when the epithelium was present.)

direction and figure 5 that in the anterior-posterior direction. The extreme variations encountered were of the order of $\pm$ 20 per cent.

It is evident from figure 4 that when only the epithelium was removed (*C*), or the epithelium together with the endothelium and Descemet's membrane (*D*), sodium chloride went through the cornea and did so at a substantially constant rate. The removal of the endothelium and Descemet's membrane enhanced the transfer rate to some extent. Other experiments in which the sodium chloride concentration in the tube was maintained constant at 50 mg. per cubic centimeter have shown that the somewhat arbitrary method of calculating the rates on the basis of a constant sodium chloride concentration in the tube is justified, for the rate of sodium chloride transfer for corneas without epithelium remained practically constant for the twenty-four hours of the experiments. In contrast to corneas without epithelium, those with epithelium (*A* and *B*) showed initially little or no sodium chloride transfer. The rate of transfer, however, increased rapidly during the first four hundred minutes and ultimately approximated the rate of transfer for corneas without epithelium.

The curious behavior of corneas from which the epithelium has not been removed has a simple explanation. As one of us (D. G. C.[12]) has previously shown, whenever the posterior corneal surface is in contact with a sodium chloride solution that is hypertonic to that in contact with the anterior surface, water will pass through the epithelium from the anterior surface and accumulate between the epithelium and the substantia propria. As a result, bullae form ("bullous keratitis"), and ultimately the epithelial layer is destroyed. Under the conditions of the present experiments these bullae were grossly visible in about fifteen minutes (fig. 6*A*); they increased in size, became confluent and raised the entire epithelium (fig. 6*B*). After about three hundred to five hundred minutes the large bullae burst and the remnants of the epithelium either fell to the bottom of the flask or hung in shreds from the margin of the cornea (fig. 6*C*). From about this time on the rate of sodium chloride transfer seemed to correspond to that for the corneas from which the epithelium had been purposely removed. It was possible to do a paracentesis on these bullae prior to their bursting and recover as much as 0.5 cc. of fluid. The salt content of this fluid was intermediate between that in the tube and that in the flask. It is significant that despite the fact that 0.5 cc. was present in the bullae punctured there was no change in the fluid level of the tube, a fact showing that the subepithelial water had passed through the epithelium in the backward direction.

When the corneal surfaces are reversed so that the anterior surface faces the salt (fig. 5), sodium chloride passes in the anterior-posterior

12. Cogan, D. G.: Experimental Production of So-Called Bullous Keratitis, Arch. Ophth. **23**:918-925 (May) 1940.

direction only when the epithelium is absent. The rate of transfer approximated that in the posterior-anterior direction under analogous conditions. When the epithelium was present practically no sodium chloride passed through the cornea. In contrast to the previous experiments, the anterior corneal surface was in contact with a relatively hypertonic solution, and neither the appearance of bullae nor destruction of the epithelium took place.

The transfer of sodium chloride following removal of the epithelium was unaccompanied by any volume change, whereas in the presence of intact epithelium there was a considerable increase in the quantity of water in the tube (fig. 2). But it is in the presence of intact epithelium that little sodium chloride is transferred, and it is possible that the transfer of water through a relatively thick membrane in one direction retards the passage of salt in the opposite direction. To test this possi-

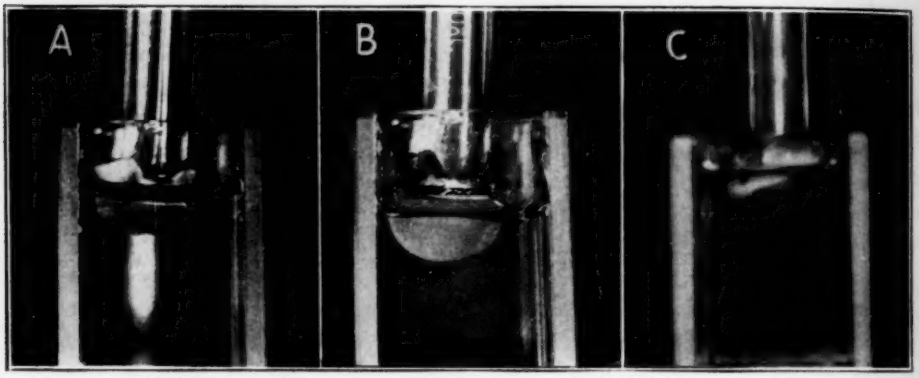

Fig. 6.—The formation of bullae after (*A*) fifteen minutes, (*B*) three hundred and fifty minutes and (*C*) five hundred minutes.

bility the diffusion of chloride [13] without simultaneous transfer of water through the whole cornea was studied by the following procedure: Two cubic centimeters of 5 per cent sodium chloride solution was placed in the tube, and 10 cc. of osmotic-equivalent sodium nitrate was placed in the flask. The experimental procedure was otherwise the same as that previously employed when distilled water was used in the flask. Analyses of the flask contents showed no appreciable amount of chlorides to be present whether nitrate solution or distilled water had been used. In another series osmotic-equivalent concentrations of dextrose were used

13. Chloride determinations have previously been used as a criterion of the amount of sodium chloride transfer. In the presence of other anions, however, it is valid to speak of chloride only, since under this condition it is not necessary to the electrostatic equilibrium that an equal amount of the cation accompany the anion.

instead of sodium nitrate, with the same result. The latter experiments were done to eliminate the influence of ion exchange. Thus osmotic transfer of water in one direction did not account for the absence of sodium chloride diffusion in the reverse direction. On the other hand, preliminary removal of the epithelium allowed relatively free diffusion of chloride into the flasks containing sodium nitrate and dextrose. The amounts equaled within the experimental error the quantities previously found to diffuse into the distilled water.

COMMENT

From the data on water transfer by osmosis the inference might be drawn that the cornea, or more specifically the epithelium, possesses a unidirectional permeability to water. Such a deduction could be based on the fact that water transfer occurred only in the posterior-anterior direction, an effect that was abolished by removal of the epithelium. But the one experimental condition wherein water was transferred was the one wherein no appreciable amount of salt passed through the cornea in the opposite direction. For this reason the failure of water transfer in the anterior-posterior direction or in either direction in the absence of the epithelium must be attributed to lack of maintained osmotic force rather than to any inherent property of the cornea which would prevent unilateral transfer. The experiments with heavy water also show beyond doubt that the cornea is permeable to water in both directions. To be sure, the transfer of heavy water was measured in one direction only, but as the fluid volumes remained constant, every molecule of heavy water that was transferred necessarily was replaced by a molecule of ordinary water coming from the opposite side of the cornea.

With regard to the mechanism of the formation of bullae, it is now apparent why the water accumulates between the epithelium and the substantia propria. It was demonstrated that the epithelium was essentially impermeable to salt and was in consequence capable of acting as a semipermeable membrane. The substantia propria, on the other hand, was permeable to sodium chloride and was not able to act as a semipermeable membrane. Thus water is passed by osmotic pressure through the epithelium and accumulates between the epithelium and the substantia propria, since there is no maintained osmotic pressure to force it through the remainder of the cornea, i. e. the substantia propria.

The necessity for continuous stirring is worth emphasizing. In preliminary experiments no allowance was made for the slowness of sodium chloride diffusion in the tube. As a consequence, particularly when salt was in the flask and water in the tube, any transferred salt formed a layer in the bottom of the tube and interfered with the further transfer of salt. As this effect increased with time, the preliminary observations

on salt transfer suggested that the permeability of the cornea progressively decreased throughout the experiment. The error of this inference was demonstrated by the adoption of the mechanical stirrer; the rate of salt transfer thereafter showed no appreciable decrease in the twenty-four hours of the experiment.

CONCLUSIONS

1. A net transfer of water through the excised cornea by osmosis can be demonstrated in the posterior to anterior direction; this transfer depends on the maintenance of the osmotic pressure by an intact epithelium.

2. No net transfer of water can be demonstrated in the anterior to posterior direction under otherwise similar experimental conditions; this absence of water transfer is due to the formation of bullae and consequent epithelial damage, which occurs whenever the sodium chloride concentration is higher on the posterior than on the anterior surface.

3. From experiments with deuterium oxide (heavy water) it may be inferred that water is transferred through the excised cornea by diffusion in both directions; the epithelium somewhat decreased the rate of transfer.

4. An appreciable transfer of chloride through the excised cornea by diffusion can be demonstrated in either direction only when the epithelium is damaged or removed; the epithelium is essentially impermeable to sodium chloride in either direction.

Miss Sally Walker and Miss Cynthia Steitz gave technical assistance in the carrying out of these investigations.

MARFAN'S SYNDROME

(ARACHNODACTYLY, COUPLED WITH DISLOCATION OF THE LENS)

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NEWARK, N. J.

Recognition of the association between ocular manifestations and pathologic changes as well as malformations in distant parts of the body belongs to one of the fastest growing chapters in ophthalmologic knowledge. Ocular changes accompanying osseous dystrophies form well circumscribed entities. Optic nerve atrophy in oxycephaly, exophthalmos and ophthalmoplegias in Apert's syndrome (acrocephalysyndactyly), optic nerve atrophy in dystrophia craniofacialis (Crouzon), optic nerve atrophy and divergent strabismus with synostosis of the major and minor alae of the sphenoid bone, blue sclera, deafness and osteoporosis causing spontaneous fractures (Lobstein's disease) are but a few illustrations. In another group of ocular changes, linkage with anomalies of the fingers is characteristic. Retinitis pigmentosa occurs with polydactyly, microcornea with brachydactyly, aniridia with dystrophy of the hands and feet or with malformation of the hands in the form of *des pinces de homard* and, finally, congenital dislocation of the lenses with arachnodactyly (Marfan's syndrome). The exact clinical observation interpreted in the light of widening knowledge of hereditary factors doubtless will lead to further enrichment of the subject.

Knowledge of congenital dislocation of the lenses and arachnodactyly began with the observations of Marfan (1896), who demonstrated a peculiar and until then never described condition characterized by a congenital symmetric malformation of the four extremities in a 5½ year old girl. This malformation consisted in a considerable elongation of the bones and in a certain degree of attenuation, more pronounced in the distal parts. There were contractures of the fingers, poor musculature but a normal reaction to electricity, a considerable spur of the os calcis and a pronounced deficiency of subcutaneous fat. The ears were well formed but with a somewhat unusual insertion. The dentition was normal. Besides, there were contractures in the elbows and in the knees and a marked retardation of the development of the locomotor functions, but no pronounced nervous disturbance. Marfan called this syndrome *dolichosténomélie* and described the fingers and toes as "spider-like."

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He considered the deformities as possibly a result of trophic alterations of neuropathic origin but also mentioned the possibility of an endocrine pathogenesis similar to that of acromegaly.

The same child was followed in her further development and presented six years later by Méry and Babonneix (1902). These authors noted the still existing difficulties in locomotion. The child could not yet walk, owing partly to some tendinous contractures in the joints and partly to insufficient education. Furthermore, there were a kyphoscoliosis in the dorsolumbar portion of the spine and a tumefaction in the elbow due to a coincident tuberculous infection. Another striking feature was the fact that the patella had not followed the growth of the femur but remained in an abnormally high position within the tendon of the quadriceps muscle. These authors proposed the name "hyperchondroplasia" in contrast to "achondroplasia," because the roentgenograms showed an unusual size of the cartilages in the epiphyses. They discussed among the pathogenic factors the possibility of syphilitic infection.

In the same year Achard described a girl 18 years of age whose condition he assumed to be similar to that in the case of Marfan and Méry and Babonneix. He emphasized the fact that the characteristic feature as shown by the measurements taken in this case was not so much an elongation of the extremities as an attenuation and only a comparative elongation, especially, of the most distal parts. He chose the name "arachnodactyly" because of the spider-feet-like aspect of the fingers and toes already described by Marfan in his case. This name was to appear most frequently in later papers on the syndrome. Achard laid greatest stress on the gracility of the extremities, on the poor development of the soft tissues and on the comparative length of the third phalanges of the fingers. In his case there was no disturbance of the locomotor functions and no contracture of any joints; nor was there any nervous disturbance or developmental retardation. The movements of the joints were even more free than usual, and hyperextension was possible in some of the joints of the hands and feet. Ossification of the skeleton was normal, with no hyperchondroplasia. Roentgenograms confirmed the fact that only the last phalanges were really elongated, while the others were only narrower than usual.

Even in these early cases the discussion started as a surmise that the condition was of a hereditary character. In the case reported by Marfan no member of the family was known to have a condition similar to the one described, but it is pertinent to note with regard to some of the biologic connections of this condition later brought out that a brother of the patient had a congenital cataract and, further, that the father was an alcoholic addict and the mother suffered from migraine and nervousness. In Achard's case the mother of the patient as well as

one of the sisters had remarkably large hands, as did the mother's father. No mention was made of any pathologic condition of the eyes in either of these first 2 cases.

The next case was reported in 1903 by Poynton as "a case of atavism." He described a boy 3 years old unable to walk properly but assuming a posture similar to that of a chimpanzee when put down on his feet: the whole body bent forward, the head bent, the hands held in front and the wrists, elbows, hips and knees flexed. In addition he described the fingers and toes as extraordinarily long owing to the length of the penultimate phalanges, the movements of the toes freer than normal, the os calcis projecting backward more than usual, the plantar arches poorly developed, the muscles of the thighs dwindling rapidly above the knees, the ligaments of the patellas elongated, the auricles large and the ridges of the conchae multiplied. It was not possible to extend the thighs or knees fully. The head was well shaped, but the palate was highly arched and narrow. It did not seem possible to explain the whole condition as the result of a persistent fetal flexion of the lower limbs. Poynton suggested a "casting back to a prehistoric ancestor." In the discussion following the demonstration, Cautley mentioned the possibility of a modified form of the infantile variety of muscular dystrophy. Voelcker suggested that the comparatively good development of the lower parts of the pectoralis major and the latissimus dorsi muscles fit well into the theory of atavism. No reference was made to Marfan and Achard. Only later was this case cited as an instance belonging to the same group as theirs.

The same is true of a case described by Peritz (1911) in his monograph on infantilism in an 18 year old girl with considerably overgrown hands and feet, underdeveloped secondary sexual characteristics and slight struma without any signs of either hyperthyroidism or hypothyroidism. The nervous system and the eyegrounds were normal, and so was the sella as shown in roentgenograms. The expression of the face and the mental behavior were infantile. Peritz designated the condition dysgenitalism with disease of the thyroid gland and partial giantism restricted to the distal parts of the extremities. No ocular symptoms, cardiac anomaly or other malformation was mentioned.

Nine years later, in the description of a similar case by Salle (1912) no reference was made to the previously described cases, and it was left to later authors to detect the connection of this case with arachnodactyly. The aspect of the case most important for the history of the syndrome is that in it for the first time an ocular symptom was reported: The pupils were narrow and the anterior chambers shallow, though the disks and the eyegrounds showed no anomaly. Another diagnostic point was mentioned for the first time, which in most of the later papers on

arachnodactyly was considered as one of the most constant features of the syndrome, that is an anomaly of the heart. Incidentally, this case is the first in which an autopsy was performed. The child, who was under observation from the first day of his life, died when 2½ months old after increasing attacks of dyspnea and cyanosis. The autopsy revealed as the most striking feature the length and slenderness of the hands and feet and the unusual form of the auricles. There was a remarkable enlargement of the sella; the hypophysis was pressed against the dorsal part of the sella by a bony tumor from the nasal side. The hypophysis itself seemed macroscopically to be unaffected, and it did not under careful microscopic scrutiny show any characteristic changes. There were comparatively many eosinophilic cells, but the picture was not that of adenoma. The heart was enlarged and dilated, and the foramen ovale was patent. The tricuspid and the aortic valve showed reddish gray elevations near the margins. The intestines seemed to be longer than normal. Salle considered the condition most likely a combination of giantism and acromegaly, a form of acromegaly modified by continued physiologic growth or, possibly, an irritation of the secretory function of the hypophysis by the exostosis at the base of the sella.

The year 1913 brought a new case in the French literature. Dubois described a 10 year old girl under treatment for congenital luxation of both hips. Both the father and the mother of the child were small, but another child of the family was tall and strong. The extraordinarily long and slender hands and feet of the patient were noticed at birth. Some years before the examination it was noticed that the beating of the heart was always violent. In size the child was average or a little below, and only her slender build made her appear tall. Medical examination disclosed a pathologic condition of the heart and also hammer toe; roentgenograms of the skull showed the sella to be of normal shape. There was no marked mental retardation.

In the year 1914 3 new cases appeared in the German literature. Thomas described arachnodactyly with webbing and deformity of the auricles in a boy 1½ years of age. The same author two years before had reported, in a monograph on giantism in childhood, a case of unusual enlargement of the hands and feet with a general precipitation of the ossification and a slenderness of the limbs not so pronounced as in this case.

In the same year Boerger called attention to 2 cases, 1 of which was also demonstrated by von Pfaundler. This case is the first in the literature in which, besides the typical length and slenderness of the hands and feet, heart failure, kyphoscoliosis, spurred os calcis and pes planus, the characteristic symptoms of congenital luxation of the lens and iridodonesis with enlarged cornea and hydrophthalmos were known

to be present. The child died when a little more than a year old, and Boerger described the observations at necropsy as follows: a small opening was present in the valvula fossae ovalis; there was abnormal lobulation of the lungs; the ceilings of the orbits protruded against the inner aspect of the skull; the sella was of unusual form, with enlargement of the alae parvae, and the hypophysis was flattened, with a shrunken surface.

Boerger's second patient was a 9 year old boy whose father was diabetic and inebriate but tall and strong and whose mother was gracile. The unusual length and slenderness, especially of the hands and feet, were noticed at birth. The expression of the face was melancholy and the behavior tearful and timid. The configuration of the extremities was typical. There were paralytic thorax with slight scoliosis, winged and boat-shaped scapulas, spurred os calcis, overextensibility of the hands and feet, bilateral genua recurvata and pes planus on the left. The muscles were poor but the muscular function good. The right bulb was somewhat prominent, there was severe iridodonesis on both sides, the anterior capsules were dull and remnants of pupillary membrane were present. There was high grade myopia (—16 D. and —20 D., respectively), the fundi were normal and the conuses were myopic. The heart was enlarged to the left, there was a loud systolic murmur at the apex and along the sternum and the second pulmonic sound was accentuated. The penis and the testes were slightly underdeveloped. The palate was highly arched. The intelligence was normal. Measurements showed that the most characteristic feature was the diminished circumference and breadth of the limbs rather than their elongation. Ossification was advanced. The orbits were deep, the anterior fossa of the cranium small and the sella somewhat large but within the normal range.

Neresheimer (1916) described a typical case. The patient was a 6 year old girl whose sister of 17 was slender and gracile. The heart was enlarged to the left, but the sounds were clear. The joints of the hands and feet were hyperextensible, there was pes planus, a calcaneal spur was present, the sella was rather flat, the orbits were deep, the expression was senile, there was no deformity of the spine and the ears were well shaped. The pupils and the fundi were normal, and there was no iridodonesis. Remnants of pupillary membrane were present. The author considered the condition a congenital, multiple, vegetative disturbance comparable to mongolian idiocy, a congenital but not hereditary aberration of the germ plasm leading to multiple dyplasias and functional inferiorities.

The next three years brought short publications by Rietschel (1917), Lust (1919) and Nobel (1919). The case of the last-named author was republished with a photograph showing remarkably well the aged and somewhat melancholy facial expression often described as characteristic.

In 1920 Thursfield published a thorough description of a typical case in which the hands and feet were unduly flexible and there were contractures of the thumbs, knees and elbow joints. The patellas were unusually high, there were severe scoliosis and pigeon breast, the scapulas were winged and there was dolichocephaly. No ocular symptoms were described.

Dupérié, Dubourg and Guénard (1921) described a 6 year old girl who was small for her age, being 82 cm. in height (normal, 115 cm.) and 9 Kg. in weight (normal, about 15 Kg.), but typical in the structure of her limbs, with spurred os calcis, kyphosis and lax ligaments. She also had congenital bilateral luxation of the hips, prognathism of the upper jaw and a highly arched palate. Remarkable in this case was the extreme youth of both parents at the time of the child's birth; the father was 17 and the mother 16. In the discussion following the paper Rocher mentioned a case of the same syndrome but formerly considered by him an instance of multiple congenital laxity of the joints in contrast to the syndrome of congenital rigor of multiple joints which he had described in earlier reports (1920).

Poynton and Maurice (1923) described a 16 year old girl with the typical syndrome and in addition progressive spinal curvature, progressive contractures of the fingers and organic heart disease, which these authors, however, considered caused by previous tonsillitis. The abnormal growth of the long bones allegedly did not start before the age of about 12 or 14 years. In the discussion following the report of this case, a "member of the medical society" (Medical Society of London) spoke of a patient under his care, a child of 12 months, with exactly the same syndrome but with congenital dislocation of the lenses also.

The first paper which stressed the ocular symptoms was published by Ormond and Williams in 1924. They described a 12 year old boy with the typical habitus, bilateral iridodonesis, dislocation of the left lens and absorption of the right lens due to a previous operation. There were a functional systolic murmur, slight webbing of the fingers and slight upward displacement of the patellas. The boy was tall, underweight and dolichocephalic, with his hands and feet characteristically long and slender. The palate was highly arched. There were absence of subcutaneous fat, acrocyanosis, winged scapulas, a prominent supraorbital ridge, contractures of the biceps and slight scoliosis. There was no evidence of congenital heart disease, but there was a functional systolic murmur in the pulmonary region and the heart was relatively enlarged in comparison with the small size of the thorax. The muscles were weak and the sella normal. The right eye showed a deep anterior chamber, a tremulous iris, a small but active pupil with a poor response to atropine and postoperative aphakia with only a small fragment of the lens capsule

in the pupil. Vision was improved with a +6.00 D. sph. Macular fixation was defective. The left anterior chamber was deep, the pupil small but active and the iris tremulous. The response to atropine was poor. There was a large myopic crescent. Vision with a —40.00 D. sph. was 6/60. There probably was backward dislocation of the lens, but the pupil did not dilate sufficiently to show the margin of the lens.

Ormond and Williams collected and discussed 16 cases from the literature and from their own experience (they counted 17, but the case of Pfaundler was identical with that of Boerger). Some ocular symptoms were mentioned in 8 of these 16 cases. The authors quoted were Marfan, Achard, Poynton, Salle, Dubois, Thomas, Pfaundler and Boerger (case 1), Boerger (case 2), Dupérié, Dubourg and Guénard, Thursfield, Rocher, Poynton and Maurice, the "member" in the discussion mentioned and Fowler (2 cases not published elsewhere).

A paper by Piper and Irvine-Jones in 1926 described a case of arachnodactyly, the first in the American literature. The patient, a 21 month old child, had also a cleft palate, a slight deformity of the ears, a deficiency of the lower eyelids, a brachycephalic head (this anomaly has been reported in the later literature, too), a congenital cardiac lesion, a delay in the motor and mental development, kyphoscoliosis and small pupils reacting slowly to light. The child died of pneumonia, and the necropsy showed, besides the other typical findings, an unusual division of the pulmonary lobes. The pituitary gland appeared to be normal, and the heart showed a deficiency in the interventricular septum. In the discussion 17 previously described cases were reviewed; the patient was female in 11 and male in 6. Of the patients, 10 had ocular abnormalities, including 5 with displacement of the lenses. In 10 the heart was normal or not described in detail; a murmur was present in 8, 5 of whom had a definite congenital defect.

Schlack (1926) described a case in which there was involvement of the central nervous system, a manifestation until then unknown. The patient, a 5 year old child, had, in addition to typical arachnodactyly, neurologic symptoms which seemed to be based on a combined malformation or degeneration of the pyramidal tracts and the posterior fascicles recalling Friedreich's syndrome. The unusual length (63 cm.) and the gracility of the extremities were noticed at birth. At 5 years of age the boy was 112.5 cm. tall and weighed 13.5 Kg. His intelligence (Binet-Simon test) corresponded to his age. The muscles were poorly developed and the joints hyperextensible, and there was spurred os calcis. There was pes cavus but also pes planus due to weakness of the arches. The eyes were deeply set, the orbital ridges strongly formed, the pupils narrow and the fundi normal. There were iridodonesis, dislocation of the lenses and nystagmus. The ears were deformed and the thorax

narrow and funnel shaped. There was slight kyphosis. The heart was enlarged to the left, and a systolic murmur and epigastric pulsation were present.

Thomas (1926) gave a report on a 2½ year old child with typical arachnodactyly combined with deformities of the auricles and webbing of the fingers.

In the same year, 1926, a paper was published by Braithwaite concerning the relation of hypertelorism to mongolism; it was pointed out that symptoms of apparent dyspituitarism in the syndrome of mongolian idiocy as well as in that of hypertelorism may be considered as secondary to a primary genetic multiple aberration.

During 1927 various casuistic reports were published. Bauer demonstrated a case of arachnodactyly with deformity of the ears; Rominger reported on a 6½ year old girl with typical arachnodactyly, an unusual senile expression of the face, kyphosis and a double row of teeth in the lower jaw. Grosser and Igersheimer described a case of arachnodactyly with typical ocular symptoms: miosis, luxation of the lenses and, in addition, moderate megalocornea. The authors expressed the opinion that the condition of the eyes was coordinated with the general disturbance in the proportions by an abnormal process of growth.

Moro reported a case of arachnodactyly combined with congenital vitium cordis and neurologic symptoms, which again recalls Friedreich's syndrome, but included among the symptoms was a considerable increase in the reflexes, especially the abdominal ones and clonus of the foot. However, these symptoms, present during a pyelitic condition, subsided at least partially when the child recovered and the general health improved. In the discussion following the report Mader described another case of pure arachnodactyly without any neurologic anomalies. This one was followed for seven years.

Ganther, describing a girl 6½ years of age with typical arachnodactylic proportions, impaired hearing and kyphoscoliosis but no ocular symptoms, denied the role of heredity. He also reviewed the literature, although not very completely, since he considered only 9 cases although the international literature until then already contained at least 30 cases. He attributed the condition in his case to the influence of a disease of the mother during pregnancy.

Brock, too, in the discussion of previously described cases, considered only the 7 in the German literature (Salle, Thomas, Boerger (2), Neresheimer, Schlack and Ganther). His patient, a girl 10 years old, showed, in addition to the typical habitus, a retardation of physical as well as of mental development. She had also a highly arched palate, habitual luxation in various joints (the mandibular radial and talonavicular joints and those of the toes), a funnel-shaped chest, scoliosis, exostoses, contractures in the finger joints, spina bifida occulta and

spurred os calcis. Brock considered the syndrome as a type of multiple congenital aberration involving, in the first line, mesenchymal structures, and he held it advisable to differentiate the picture of sporadically occurring, marked degenerative conditions of this kind from the familiar picture of a narrow build. With this point of view he stood out in the following years in contrast to authors with a broader outlook who described arachnodactyly as of comparatively frequent occurrence and in genetic connection with familiar types of slight or more pronounced slenderness. The part played by the mesenchymal structures within the constitutional pathologic disturbances was studied thoroughly in a paper by Staudenath (1928) but without special reference to the question of arachnodactyly.

Other causuistic reports were published during 1927 by Zuber and Baessler and Schneider and during 1928 by Zuber and Cotenot, Bier, Kallius and Schreiber, Duhem and Jubert. A case briefly mentioned by Hamburger was noteworthy for the narrowness of the region of the sella turcica. Reports appeared in 1929 by Thaden with special emphasis on the ophthalmologic findings; by Wagner; by Mueller, who discussed arachnodactyly in its relation to other degenerative conditions, and by Young, who analyzed especially the various ocular findings in the cases of arachnodactyly until then reported. His summary listed, among 26 cases, 9 reported without any mention of a special ocular condition and 13 in which there were ocular abnormalities. In 7 cases there was dislocation of the lenses, in 5 iridodonesis, in 5 small pupils and in 4 deeply set globes. Young added 4 new cases, with exact measurements. Two of the patients were brother and sister in a family in which the mother showed similar features, including dislocation of the lenses. The other 2 patients showed features of amyotonia congenita; in one the condition was only slightly suggested and in the other it was more pronounced.

The year 1930 brought a report of a case by Schrader remarkable because of the family history and as a typical example of the degenerative type. The patient, an 18 year old youth, was the product of incest between father and daughter. In the same year de Haas published a report on 2 patients in the Netherlands East Indies, a brother and sister, with arachnodactyly and ectopia lentis.

During the next years most of the reports appeared in ophthalmologic literature. As soon as the connection between ectopia lentis and arachnodactyly was more generally known, oculists considered the possibility of this syndrome in each instance of congenital displacement of both lenses and these reports became more frequent. A thorough and scholarly investigation was published by Weve in 1931. He emphasized the special part played by a fetal disturbance of the mesodermal structures in the pathogenesis of the syndrome and 16 cases, in some

of which, however, only a few features of the syndrome were present. Especially interesting is the fact that the greatest number of the cases occurred in only three families, in which there was a marked hereditary taint. Since Weve's publication, arachnodactyly has frequently been referred to as dystrophia mesodermalis congenita, type Marfan. The changed nomenclature of Weve was not generally accepted. Similarly, Pfaundler wanted to substitute, for arachnodactyly, acromacria in contradistinction to acromegaly, the former being marked by slenderness of the bones and underdevelopment of the soft tissues. The attempt of Laval to establish the terms dysmesdactyly for cases in which structures of mesodermal origin are involved and dysmesectopia for cases in which structures of ectodermal and of mesodermal origin are simultaneously affected was not given recognition by later authors.

Other papers dealing with the whole complex from the ophthalmologic point of view were published in the same and in the following year by Vogt, Ringelhan and Elschnig, Franceschetti, Dor, Weill, Abelsdorff, Hudson and Padovani. Ingram and Inglis described a case of arachnodactyly with muscular hypotonia. Killmann reported 8 cases; in 7 there was typical arachnodactyly and in 1 the syndrome was incomplete. Two of the patients were female and 6 male. One had the round form of head, and the other 7 were typically dolichocephalic. The 7 patients with the syndrome in classic form also had typical ectopia lentis. One with the forme fruste was the father of a patient with the typical syndrome. Two other patients were father and son, and 2 were mother and daughter.

A new point of view concerning the possible pathogenic mechanism of arachnodactyly was presented by Passow (1934 and 1935), who stressed the close relation between the symptoms of arachnodactyly and those of syringomyelia and of the conditions now frequently considered formes frustes of syringomyelia and described under the name status dysraphicus.

During later years the papers on arachnodactyly, besides adding new casuistic data, mainly considered the following actual problems: the question of heredity and the possibility of prenatal influence, the role of the endocrine system, the theory of Marfan's disease as a systemic anomaly of the mesodermal structures (Weve), Passow's theory of myelodyspasia and the possible linkage of the condition to other congenital multiple aberrations of the constitution as they appear, e. g. mongolian idiocy, hypertelorism, acrocephalosyndactyly and the Laurence-Moon-Biedl syndrome. In recent years there has been frequent controversial discussion over the relation of the complete syndrome of arachnodactyly (including anomalies of the eyes, ears and heart and malformation of the bones, as well as unusual conditions in the joints, the typical abnormal proportions and anthropometric

conditions and the typical aspect) to the formes frustes (consisting of only part of the characteristics). The connection of arachnodactyly with internal diseases and a disposition to such diseases is another interesting subject, discussed recently by Futcher and Southworth.

As to the therapeutic possibilities, many different suggestions have been published, influenced of course by the branch of medicine to which the author of the paper belonged. In ophthalmologic literature, naturally, the possibilities in operative and in conservative methods for the amelioration of the frequently disturbed ocular function are described and discussed from different angles. Medical and pediatric papers, on the other hand, consider the chances for endocrine treatments and the prognostic outlook from the viewpoint of complications in the internal organs. In surgical and orthopedic journals one finds important suggestions for alleviating the restrictions of locomotor functions.

The etiologic explanation of the syndrome is closely related to the question of the diagnostic delimitation of the manifestations and to the question of the best and most suitable nomenclature. Looking through the entire literature, one finds that the later descriptions of arachnodactyly are inclined to stress the general aspect and the frequent, though rather variable, combination of the typical aspect with other degenerative changes, malformations or organ inferiorities. One gets the impression of a syndrome which when completely developed shows a considerable increase in the length of the extremities, especially of the hands, fingers, feet and toes, with a decrease in breadth due to slenderness of the long bones as well as to a lack in development of fatty tissue and to a smaller than normal amount of muscle. The general growth of the body shows in most, but not necessarily in all, typical cases an increased rate, producing a tall, slender type which may be classified among constitutional systems as asthenic or leptosomatic. To these features may be added some abnormalities of the connective tissue and its derivates resulting in overextensibility of some joints and contractures or hyperrigidity of others. Furthermore, there may occur facultative or habitual luxations in various joints; rather regularly some secondary changes in the spine, such as kyphosis and scoliosis; disproportions between the different parts resulting in unusual correlations, such as abnormal highness of the patellas and enlargement of the elbows; exostoses, and frequently, a calcaneal spur. The general type of bodily structure comprises mainly, but not always, a certain shape of the skull (dolichocephalic) and of the face (long and narrow), with a characteristic facial expression (aged and rather earnest or sad) and eyes deeply set. Often the palate is highly arched, and it is sometimes cleft. The jaws may have narrow arches, usually with secondary malposition of the teeth and sometimes with malocclusion.

Of great clinical importance are the malformations of the eyes, comprising congenital luxation or subluxation of both lenses, hypoplasia of the irises, miosis of the pupils, the presence of remnants of pupillary membrane and, in addition to the dislocation of the lenses, a true myopic elongation of the bulbs and myopic conuses. Some authors have described a defective structure of the irises and others a defect of the dilatator muscles with well developed sphincters of the pupils (Rambar and Denenholz, 1939), which may point to a certain period of embryonic life during which the deviation from the normal took place.

As for the internal organs, there are important pathologic findings concerning the heart, especially the presence of an open duct of Botalli or an open foramen ovale. In some cases there is probably some kind of congenital inferiority of the heart structure which favors the development of rheumatic or other postinfectious heart failure. In some cases the lungs show aberrations in the formation of the lobes and a special disposition to pulmonary disorders.

Besides the typical cases, in which the syndrome is fully developed, there are abortive cases, in which a more or less impressive habitus recalls the typical picture but other characteristic symptoms are absent. It is questionable whether or not such cases should be included in the diagnostic group with those of typical arachnodactyly. This problem won new life by the controversy over the hereditary character of the syndrome and—heredity being assumed—over the type of transmission. Those authors who emphasized the hereditary character of the syndrome often based their opinion on the occurrence of such incomplete or abortive cases in a family in which a true and completely characteristic case appeared. The opposing faction held that there is no justification for including in the entity of arachnodactyly more or less pronounced slenderness of the body or of the extremities without other striking features.

I believe that it may be possible even in the light of modern experiments in genetics to bridge over this controversial point of view. It is known today that there are conditions which result not from the effect of a single hereditary gene, or representant, but from the collaboration of two or more such genes, or genetic factors. Pathologic changes sometimes include a wider and sometimes a narrower district in the groups of symptoms which show relationship to each other. The material basis of such events is the structure and organization of the chromatin particles within the cells. Experiments with animals have given evidence that it is possible, by means of the science of probability and variations, to find certain rules which prove the connection between the coincidence of combinations among different symptoms and the position of the representants of these symptoms within the chromosomes. One may assume

as a consequence of these recent experiments in the field of genetics that there are also pathologic variations which may comprise in one case a larger and in another case a smaller part of a single chromosome and may be extended at times more to one side and at times more to the other side. So one can understand that there is a certain symptom complex grouped around a central symptom, in this case extreme slenderness of the extremities. Accordingly, variable, far reaching damage to another part of the same chromosome, reaching sometimes more to one side and sometimes more to the other, could result in the variations seen in the different cases of the typical syndrome. Symptoms such as slenderness may be effected, however, by the collaboration of different genetic factors, even if one considers only the slenderness of the long bones (plurifactoral symptoms). On the other hand, it is known that simple genetic factors are probably able to influence simultaneously different qualities (pluripotential factors). When applying this knowledge to the problem of the variability of such a syndrome as arachnodactyly, one has to consider the possibility of two or more typical symptoms being caused by the same material corpuscle (pluripotential gene) or by near lying particles, or genes, which are damaged together because of proximity.

Again, according to the theory of gene exchange, in a certain biologic phase, the chromosome conjugation, or the synapsis, a process in the ripening act of the germ cells, some particles within the chromosomes change connection with their neighborhood. This explains another possibility of changing combinations in genetic happenings. Changing combinations in the transmission of hereditary qualities were the basis for the construction of the so-called chromosome maps, which give a survey of the supposed position of the representants, or genes, within the single chromosome of the subject most often used in genetic experiments, Drosophila. One can imagine that merely the fact of various combinations occurring in such a syndrome as arachnodactyly can give a hint as to the probable position of the representants of the concerned qualities within the chromosomes in man. That the different single symptoms often combined in Marfan's syndrome are caused not by multipotential genes but by genes located close to one another within the same chromosome is a plausible conception because of the frequent but not general occurrence of the combinations. If there were a pluripotential gene common both for slenderness of the extremities and for luxation of the lenses, it would be impossible to understand why this combination would be present in some cases and absent in others. The combination or lack of it is explained more easily on the basis of genes located near each other within one chromosome, so that damage may be done to both factors in one case but to only one of them in the other case.

One can also imagine, for example, that the gene for slenderness of the extremities may be located between the gene for subluxation of the lenses or for the underlying embryonic processes on the one side and the gene for disturbed cardiac development on the other side. An almost mathematical analysis would permit one to determine from the frequency of a single symptom and of combinations of symptoms the position of the representants, or genes, within the chromosome.

The question would naturally arise whether or not there is a typical combination of congenital luxation of the lenses and open foramen ovale, or of open duct of Botalli and an ear deformity, with a physical structure opposite to that of arachnodactyly, that is a stout broad body with short broad extremities. The question is complicated on the one hand by the fact that there remains the possibility of the cooperation of more than one gene to produce the effect of a certain phenotype and on the other hand by the fact that some symptoms are effected by the collaboration of different embryonic processes, each of them based on different genetic factors.

CLINICAL FEATURES OF MARFAN'S SYNDROME

Recent research has given unmistakable evidence that ectopia lentis and spherophakia are relatively often combined with arachnodactyly and other malformations. The chief clinical features must be subdivided into (*a*) skeletal, (*b*) general and visceral and (*c*) ocular defects.

Skeletal Defects.—In the majority of cases the skull is dolichocephalic (but cases of brachycephaly have been reported by Piper and Irvine-Jones and Carrau). There are prominence of the supraorbital ridge, bossing of the frontal eminences, a broad and sunken nose, a narrow palatal arch, occasionally cleft, and a prominent massive chin. A certain degree of hypertelorism is sometimes present. The external ears are frequently malformed, protrude from the head in their upper part and show enlargement of the lobes. The teeth may be long and narrow, but in a few cases a double row of teeth has been seen. The face is thin and the skin often wrinkled. The prematurely aged, melancholy or pained expression has been repeatedly described. The limbs are exceedingly long and slender. There is not only a real increase in the length of the extremities as compared with those of normal children of identical age but a relative increase in comparison with the weight, and there is a disproportion between the length of the extremities and the height. The span between the tips of the middle fingers with arms extended often outstrips the height and represents one of the typical aberrations. Thus, the arms may reach almost down to the knees. To illustrate the abnormal but characteristic growth of the body, a few instances from the literature should be given: Albanese's patient, a girl of 13, was 164 cm. tall with a span of 177 cm. between the extended fingers. The patient of Dvorak,

a girl, was 5 feet 9¾ inches (177 cm.) tall at 14 years and 5 feet 10½ inches (179 cm.) tall at 24. Killmann's patient 8, a boy of 11, was 168 cm. tall. The 12 year old boy in Francois's report measured 158 cm. and had a span of 165 cm. One of Lloyd's patients, a boy of 15, was 150 cm. tall, with a span of 170 cm.

The metacarpal bones and the phalanges show a well defined increase in length, which in some cases is relatively greatest in the terminal phalanges, giving to the fingers the delicate spider-like appearance described in Marfan's first case. The skeletal changes differ from those in giantism and acromegaly, in which both thickness and length are increased. In arachnodactyly the roentgenograms show no true pathologic changes in structure, the bones being simply elongated, though the presence of epiphyses at the proximal and distal ends of the first and second metacarpal bones and of all the phalanges may be revealed. The feet also show an elongation, owing to long and slender metatarsal bones and toes; of the latter, the outer three often show an inward deflection of the terminal phalanges. The peculiar configuration of the feet causes the inconvenience of needing shoes made to order.

Of the thoracic deformities encountered, the funnel-shaped chest is the most common, but the pigeon breast type with narrowness and flattening of the chest wall is often seen. Some degree of kyphosis and scoliosis and winged scapulas are found; these deformities are probably not congenital but the result of defects in muscular development and weakness of the vertebral ligaments. Spina bifida occulta has been noticed in a few instances (e. g. in the case of Zuber and Cotenot and in Weill's eighth case). Laxity of the joints and ligaments, particularly of the elbows, fingers and knees, forms a constant part of the picture. This may be so marked as to permit actual subluxation. When contractures are found, there may be inability to supinate or to extend fully the thighs or the fingers. An abnormally high position of the patella was described by various authors. Spur of the os calcis, pes planus, hammer toe and clubfoot, as in Friedreich's ataxia, are found. The arachnodactylic habitus is extremely obvious. In apparent contradiction, Weill described the combination with dwarfism with bilateral dislocation of the lenses and calcification in a woman 38 years of age whose height measured only 145 cm.

General and Visceral Defects.—The muscular tissue is generally poorly developed, with striking hypotonia which may suggest amyotonia congenita. The subcutaneous fat is markedly underdeveloped, which accounts for the emaciated appearance and accentuates the already unnaturally long extremities. Next to the frequency of ocular anomalies is the presence of cardiac disease. There may be a congenital defect, such as patent foramen ovale or incompetent valves, or valvular disease

acquired subsequent to endocarditis. A tubular or displaced heart may be the result of thoracic deformities. Enlargement of the area of dulness or a systolic or presystolic murmur may be present. In a few cases deformities of the blood vessels, for instance of the abdominal aorta, have been described. Pulmonary changes were observed in the few cases in which autopsy was done (in children, Salle, Pfaundler, Schmincke and Rambar and Denenholz; in adults, Piper and Irvine-Jones and Weill), such as a defect of the middle lobe of the right lung, a small middle lobe of the right lung with the left lung consisting of only one lobe or a right lung consisting only of two lobes. As a rule the nervous system escapes implication. The general intelligence is often particularly good. No involvement of the genitourinary system has ever been described. Abnormal length of the intestines has been noted (Salle).

Ocular Defects.—Ocular complications are ectopia lentis, iridodonesis, miosis, a feeble response to atropine and shallow or uneven anterior chambers. Occasionally, divergent or convergent strabismus (divergence in the cases of Fowler and Killmann; convergent in the cases of Rominger and Zuber) or nystagmus of some type is present (Stewart).

Lenticular myopia is usually found if the lens is still behind the pupil, although axial myopia may occur. The myopia in some instances has been reported as high as from 40.00 to 60.00 D. The increase of refraction in congenital dislocation is usually due to the smallness of the lens. Keeling reported 32.00 D. of myopia which after the extraction of the lens was corrected by a + 14.50 D. sph., a change of refraction due to ectopic lens of 46.50 D. Jennings found — 35.00 D. in the pupillary area containing the lens and + 11.00 D. in the aphakic part, a difference of 46.00 D. in refraction. Tikhomirov's patient showed — 33.00 D. with + 6.00 D. in the aphakic part, a difference of 39.00 D. All these corrections were determined with the strength of the correcting lens placed about 20 mm. in front of the optical center. In view of the difference between the corrective lens myopia and the calculation values, the refractive power of the lens must have been reduced, according to Ringelhan and Elschnig, in Keeling's case from 46.50 to 30.00, in Jenning's case from 46.00 to 30.00 and in Tikhomirov's case from 39.00 to 25.50 D. Thus the patients exhibited an average of 28.00 D. of refractive power of the lens, which represents 14.00 D. more than the average refraction difference of an aphakic eye formerly of emmetropic habitus.

In addition to the lenticular myopia, axial myopia may be present with the usual myopic changes in the fundus. In cases of arachnodactyly associated with dislocation of the lens, myopia was frequently noted. Boerger mentioned myopic conus, Young (case 3) high myopia and Dvorak myopia of 18.00 D. In Franceschetti's case vision in the right

eye was corrected by a — 35.00 D. sphere and the left eye by a — 13.00 D. sphere combined with a — 3.00 D. cylinder, the right eye having a myopic conus of 1 and the left eye a myopic conus of ½ disk diameter. In the author's opinion there was not only lenticular myopia but myopia representing a degenerative stigma. Myopic conus was described by Weber as slight (case 2) and by Becker as extreme (case 3). Furthermore, it was found in the cases of Schilling and of Fischbach. Isnel-Hakami, Kurz, Goedl (only in the right eye), Huber-Lièvre and Hector and Rambar and Denenholz, similarly, mentioned the presence of myopia. Hypermetropia, even of low degree, seems infrequent.

From the general literature on ectopia lentis not associated with arachnodactyly (the association was unknown at that time), it is known that the dislocation is bilateral except in the case of unilateral malformations. The dislocation is always in the vertical plane, not in the parallel, but in symmetric direction to the main axis of the body. Exceptions to the rule are the cases of Hoog, Dickey and W. Fox, in which the dislocations were asymmetric. In the first case one was downward and inward and the other downward and outward (therefore they were parallel); in the second case one was upward and the other upward and inward (absolutely atypical), and in the third case one eye showed a lateral and the other a downward displacement. Ringelhan and Elschnig listed twelve dislocations in the same direction, one asymmetric and one atypical.

A summary of arachnodactylic dislocations shows the following directions: inward and downward in the right eye and downward in the left eye in Fowler's case, nasalward in Weve's fourth case, toward the temple and outward in Nicolo's case; downward and nasalward in Killmann's second case, upward and outward in Killmann's third, fourth and fifth cases, upward and nasalward in the right eye and into the vitreous in the left eye in Killmann's seventh case, downward in Killmann's ninth case, outward and upward in Lloyd's first case, upward and inward in King's first case, upward in King's second case, lateral in the right eye and upward and outward in the left eye in King's third case, upward and outward in Becker's first case, inward and upward in Becker's third, fifth and seventh cases, downward and outward in Burch's first case, upward in Burch's fifth and seventh cases, upward and backward in Burch's third and fourth cases, downward and toward the temple in Burch's sixth case, upward and nasalward in Burch's eighth case, upward and backward in both cases of Villard, Viallefont and Temple, and upward and inward in Stieren's case.

The dislocation is usually incomplete, but it may develop into the complete form; it is usually into the anterior chamber and followed by secondary glaucoma. (Dislocation into the anterior chamber of the right eye was noted by Fleischer and by Lloyd and into the vitreous in Weve's

first case and in Killmann's first and seventh cases. Pino, Cooper and Van Wien's publication adds 1 case for each possibility.) The dislocated lens may be normal in size for the eye, or it may be decidedly smaller (Weve, Fleischer, Grosser and Igersheimer, Thaden, Bakker and Lloyd in the second case in his second publication). Opacities of various sizes and densities have been described. Ectopia of the lens may be associated with spherophakia, but according to Vogt the two conditions may occur separately. Spherophakia is mentioned by Nobécourt, Cathala and Temerson and by Dracondaidis. Weve described in his fourth case a maximally curved lens. Killmann (cases 3 and 9) and Bueckler (case 2 in his first publication) described the lens as globular.

In some cases the eyes were characterized as deep set (Schrader, Weve in his tenth case, Christophersen, Lodi, Westendorff). A peculiar slanting palpebral fissure with the outer corner in a lower position was described for the first time by Rietschel and was found in one of Kurz's cases. Hydrophthalmos was mentioned in Pfaundler's case. Dislocation of the lens was associated with megalocornea in the cases of Grosser and Igersheimer, Fleischer and Giraud, Bocca, Jayle and Mockers; with a small cornea in 1 of the cases of Lloyd (second publication, first case), and with microcornea in the case of Isnel and Hakami. Malbrán and Pícoli observed a combination with microphthalmos in 3 cases. The most usual of the congenital anomalies associated with dislocation of the lens is the presence of remnants of pupillary membrane (Boerger, Neresheimer, Nicolo, King, Calogero, Charamis, Goedl and Lloyd); coloboma of the lens is less frequent (Weve, Waardenburg, Franceschetti and King). Coloboma of the lens and iris was described by Goedl and in 4 cases by Weill; coloboma of the iris, lens and choroid was described by Goedl. Calcification of the dislocated lens was present in the seventh case of Weill.

The absence of any visible pathologic change in the zonula is mentioned in the 3 cases of Villard, Viallefont and Temple. Likewise, the zonula was found normal by Becker; Lloyd in his first case described clear and strong zonular fibers. Conversely, Buecklers found aplasia of the zonula. In Franceschetti's case (coloboma of the dislocated lens) the zonular fibers were present, and accordingly an ectodermal disturbance was assumed, contrary to Weve's opinion that the aplasia of the zonular fibers results from persistence of mesodermal tissue or rupture of the fibers in early infancy.

The arachnodactylic dislocation in 2 cases of Passow was associated with heterochromia iridis. In the first case, even the breast on the side of the lighter-colored iris was found to be smaller. Heterochromia iridis was also found by Ennema and Charamis. Aniridia of one eye and coloboma of the iris of the other eye in a brachycephalic child were described by Nobécourt, Cathala and Temerson. Atrophy and discolora-

tion of the iris occurred in 1 of Weve's cases. Dislocation in association with arachnodactyly seems to have been bilateral except in a case of Roch and 3 of Malbrán and Pícoli; in the case of the last-named authors the dislocation was associated with microphthalmos.

The histologic study by Dvorak-Theobold of an eye from an arachnodactylic child showed an incomplete separation between the iris and the trabeculae, especially on the nasal side of the bulbus, where the trabeculae and the canal of Schlemm were not well defined. The iris showed only an occasional rudimentary crypt of Fuchs, a well developed sphincter (fourth fetal month) and an undeveloped dilator muscle (this develops after the sixth fetal month). The posterior layer of the pars iridica retinae was pigmented only over the pupillary half of the iris. From the unpigmented cells there was an occasional extension of fibers toward the ciliary processes. The pigmentation of the posterior layer of the ectodermal iris occurs from the third to the seventh fetal months, and accordingly the occurrence of the abnormality and the arrest of development were placed between the eighth week and the sixth month of fetal life. The measurements evidenced the presence of axial myopia in a 2½ year old child (the case was apparently the same as that of Rambar and Denenholz). The findings of Dvorak-Theobold contradicted Futcher and Southworth, who expressed the opinion that the miosis and feeble pharmacologic response of the pupil are due to fibrosis of the iris rather than to faulty development of the dilator muscle.

A rare combination of typical arachnodactyly with dislocation of both lenses, blue scleras, deafness and osteoporosis (Lobstein's disease) was observed by Ellis. There were 4 children in the same family with blue scleras, and 1 of them, a girl 8 years old, had the symptoms of both the Marfan and the Lobstein anomalies. The blue scleras were transmitted through the father and the arachnodactyly through the mother.

HEREDITARY AND FAMILIAL TENDENCIES

The hereditary origin, or familial occurrence, of arachnodactyly combined with dislocation of the lenses as well as of each condition separately, is well established. Young was the first to describe a brother and sister (cases 3 and 4) with dislocation of the lenses; the mother of the children likewise suffered from dislocation of both lenses and had a similar habitus. Previous to Young, Achard had described arachnodactyly in 2 sisters whose mother and mother's father had similar features, so that hereditary involvement could be shown, but the cases were not typical. De Haas observed bilateral ectopia lentis in a brother and sister whose father had no dislocation but had very long hands and feet.

Weve's first family group consisted of a father, 2 sons and a daughter, all with dislocated lenses and arachnodactyly, the last member having

small, curved lenses. The grandfather apparently suffered from arachnodactyly too. In another family of Weve's a man with dislocated lenses had 16 children; 5 died, 4 having been reported as of arachnodactylic habitus. Of the 11 living children, 3 (2 boys and 1 girl) exhibited arachnodactyly and ectopia lentis. Custodis described a father and son afflicted with the syndrome. Hereditary evidence was definitely present in 2 of Weill's cases, while in Franceschetti's case of ectopia combined with coloboma of the lens, the father was described as having only unusually narrow hands and feet. Two sisters observed by Kurz had no history of a hereditary factor. In Killmann's first case a father and son showed the typical combination; the father and grandfather had only vitium cordis and a similar habitus. In a second group a mother and daughter showed arachnodacytyly and ectopia, the mother's father having had a forme fruste.

Viallefont and Temple found in their genealogic trees dominant inheritance characteristics (Weve) as opposed to recessive (Frontali). Lloyd saw the syndrome in 4 of 6 siblings; the mother and the father had similar skeletons but no ectopia. Weber described the combination in a brother and a sister of 14 siblings (6 died, and 6 were normal). Amsler examined 7 persons in three generations of one family with dislocated lenses, and in the discussion on his paper Jayle reported familial cases of dislocation with tall stature. In King's case the mother had dislocation of both lenses and the 2 daughters bilateral dislocation but combined with coloboma of the lenses. In Becker's case the afflicted mother had 1 normal son; 2 other sons and 3 grandchildren (2 of them twin boys) inherited the full syndrome. Buecklers reported on 2 sisters and Burch on a family in which the father, 2 sons and 1 daughter were affected. In the discussion Beigelman described 12 persons belonging to two interrelated families as having arachnodactyly and dislocation of the lenses. The family originated in the intermarriage of second cousins afflicted with the condition. Three of the 4 sons inherited the syndrome, only 1 child in the third generation being free. The grandmother of the family had a sister with Marfan's syndrome. Her daughter and 1 of the 2 grandchildren showed the inheritance. The grandparents had lenses dislocated into the vitreous; 2 of the 4 brothers in the second generation had lenses dislocated into the vitreous, and in the third generation partial ectopia was reported. Curschmann reported iridodonesis only in brother and sister; Delord and Viallefont, the typical combination in father and son. One of the cases of Lloyd was similar, while another case demonstrated the dislocation in mother and daughter, although the mother, remarkably enough, not only did not exhibit the typical growth of the body but, on the contrary, was short and plump (a transmitter with the incomplete syndrome). Malbrán and Picoli described 2 sisters

with the typical syndrome; their brother had dislocated lenses, and their father and his 2 brothers were of a similar type. Another group of patients (reported on by the same authors) included 3 sisters with microphthalmos and unilateral dislocation. Buecklers mentioned several persons with arachnodactyly and dislocation of the lens in one family; Schmieding, 2 children in one family, and Passow and Roemmelt, a mother and 4 children of 5 affected.

The hereditary transmission is the same in cases of arachnodactyly without dislocation of the lenses (Schwarzweller and Roederer).

On the other hand, there is a long list of cases, including some even in recent literature, in which the attention paid to a hereditary or familial occurrence was keen and apparent. Many of the cases were reported by authors who had described the same factor in other cases and are therefore of great importance. In this group belong the cases of Patterson, Coppez, Isnel and Hakami, Passow (2 cases), Benedikt, Calogero, Chiari, Morard, Kurz, Schilling, Westendorff, Charamis, Pino, Cooper and Van Wien, Roch, Roederer, Apert, Cockayne, Buecklers (2 cases), Laval, Nobécourt, Cathala and Temerson, Moore, Rambar and Denenholz, Stewart, Stieren and de Saint-Martin (a somewhat atypical case).

Ellis' observation brings up the unusual combination of blue scleras and Marfan's syndrome, the former transmitted through the paternal and the latter through the maternal strain. Just as unusual is Weill's case in which an adult female dwarf with ectopia transmitted the dislocation with typical arachnodactyly to her child. That ectopia lentis may be hereditarily transmitted without arachnodactyly was vividly illustrated by Kredbová.

The possibility of dominant inheritance was stressed by Weve, whose 23 cases occurred in six families. Of the six families, the dominant inheritance was proved in four and suspected but not determined in two. Weve established the fact of dominant inheritance by confirming the type of formes frustes, members of the same families presenting only a few of the symptoms of the complete syndrome. The importance of family search cannot be stressed enough, but, on the other hand, it may bring misleading conclusions when mere tall stature is interpreted as arachnodactyly.

The literature and the cases reported here demonstrate that the syndrome often appears sporadically, with a history completely negative as to family occurrence. When Bauer's explanation for the sporadic cases, that is mutation of the germ plasm, is accepted, following up these cases becomes extremely important. The mutation of the germ plasm, once established, is inherited, and therefore study of the descendants in sporadic cases of the complete syndrome should be one of the most important subjects of the future.

REPORT OF CASES

Ten cases of dislocated lenses were observed. In 7 of the 10 there were unmistakable signs of arachnodactyly; the remaining 3 could not be classified even as instances of formes frustes. In 1 of the latter the patient was first seen at the age of 6 months because of a high degree of convergent strabismus. Clinically and roentgenogically there were no skeletal changes from the normal. The child was followed for seven years and had developed into a relatively small person with not even a suggestion of arachnodactylic skeletal changes. The other 2 patients with normal or rather short bodies were 16 and 19 years of age and

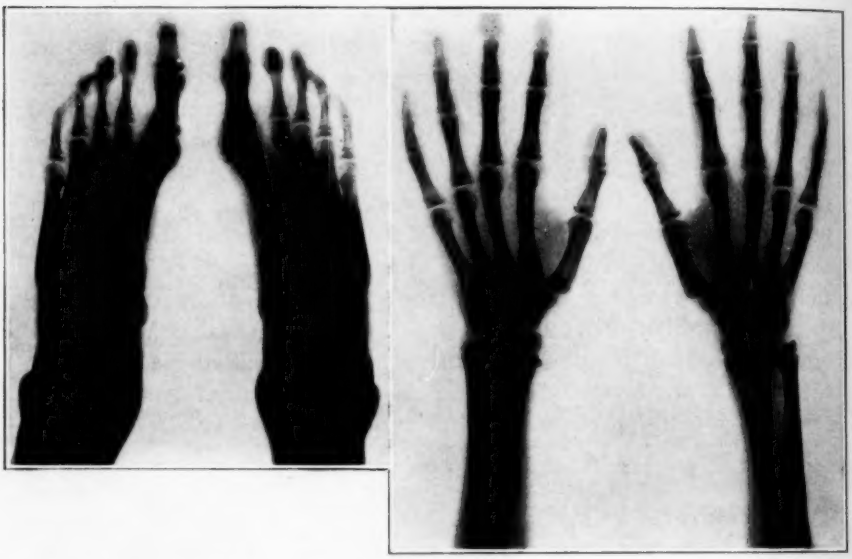

Fig. 1 (case 1).—Roentgenograms showing the marked elongation of the toes and fingers.

had typical dislocation of the lenses, but the general examination failed to reveal any changes which could be interpreted as arachnodactylic. The remaining 7 cases are reported hereafter.

CASE 1.—The patient, a boy 12 years and 2 months of age, was 59½ inches (151 cm.) tall and weighed 71½ pounds (32.4 Kg.). There were marked iridodonesis and downward and temporalward dislocation of the lenses. The visible nasal outline of the lenses was smooth, without any notching. There was myopia of —10.00 D. in the right eye and of 14.00 D. in the left. No myopic changes were seen in the fundi.

Examination of the sella turcica showed it to be a shade small, with the clinoid processes in close approximation though not actually bridged. Exposures directed to the extremities showed no gross abnormality in detail or in outline of the osseous structures. It was observed, however, that the fingers and toes

were extremely elongated. The diagnosis was small sella turcica and elongated fingers and toes (Dr. J. Furst). There was no similar case in the family.

CASE 2.—The patient, a boy 14 years of age, was 63 inches (16 cm.) tall and weighed 96 pounds (43.5 Kg.). There were severe iridodonesis and upward dislocation of both lenses. The pupils dilated poorly, and zonular fibers were not visible. The fundi were normal. Slight myopia was present. Roentgenologic examination of the skull (Dr. J. Furst) showed the sella turcica to be rather small, with the clinoid processes actually bridged. Exposures directed to the extremities showed no gross abnormality in detail or in outline of the osseous structures. It was observed, however, that both the fingers and the toes were extremely elongated.

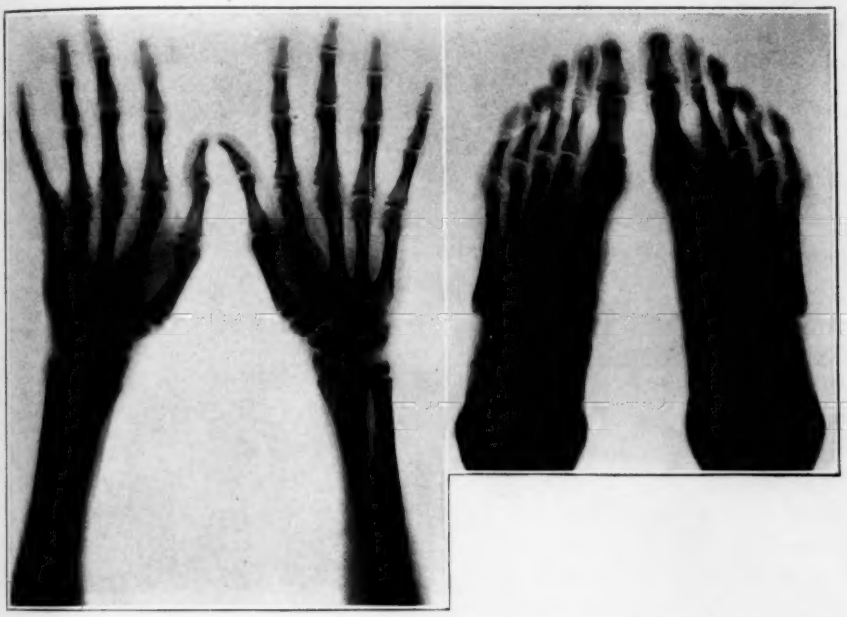

Fig. 2 (case 2).—The pronounced elongation of the digits of the hands and feet is clearly visualized.

CASE 3.—The patient, a boy 9 years and 1 month of age, was 54 inches (137 cm.) tall, with a span between the outstretched fingers of 55½ inches (141 cm.), and weighed 66 pounds (29.9 Kg.). There were severe iridodonesis and upward dislocation of both lenses. The lenses were clear and transparent, with no notching. The pupils responded poorly to mydriatics. The fundi were without pathologic or myopic changes.

Roentgenologic examination of the skull (Dr. J. Furst) revealed the sella turcica to be of comparatively normal dimensions and smooth in outline. It may be worthy of note that the skull was ovoid in type, a shade large in its transverse dimension. Exposures directed to the long bones showed a slight increase in the porosity, with further thinning of the cortices. There was also a tendency to lengthening of the fingers and toes.

CASE 4.—The patient, a boy 10 years of age, was 58 inches (147 cm.) in height, with a span of 59 inches (150 cm.) between the outstretched fingers, and weighed 69 pounds (31.3 Kg.). There were iridodonesis and a slight downward and temporalward dislocation of the lenses. The zonular fibers were invisible and the

Fig. 3 (case 4).—Visible elongation of the fingers.

Fig. 4 (case 5).—Photograph showing the elongation of the arms, which reach almost to the knees, and a comparison of the hands and feet of the patient with those of a normal adult woman (5 feet 3 inches, or 160 cm., tall).

pupils small, with almost complete lack of response to atropine. The fundi were normal. There were no myopic changes. The vision was 15/30 in the right eye with a —8.00 D. sphere and 15/20 in the left eye with a —7.00 D. sphere combined with a —2.00 D. cylinder, axis 135. The lenses were clear, and there was no coloboma. The patient was the only child of parents of short and heavy build.

Roentgenologic examination (Dr. J. Furst) showed a normal sella and pronounced elongation of the fingers and toes.

CASE 5.—The patient, a girl 4 years and 5 months of age, had a short rough systolic murmur at the apex of the heart, perhaps with slight dilatation to the left. Otherwise the internal findings were normal. There were a slight deformity of the chest, genu valgum, no marked scoliosis and no spur of the os calcis. The auricles were of unusual shape, the inferior crus anthelicis, especially, being high.

The pupils were small and dilated poorly after atropinization for three days (instillation nine times of 2 per cent atropine sulfate solution). The right eye, with vision of 15/15, did not accept correction; the left eye had vision of 10/200 or of 15/100 with a —10.00 D. sphere. The right lens was not dislocated; the left was dislocated upward and temporalward. The fundi were normal. There was pronounced divergent strabismus of the left eye. In each eye there were a few star-shaped brownish pigmented remnants of pupillary membrane.

The anthropometric measurements are shown in table 1.

The patient had a tall body with basic proportions which seemed infantile if considered in comparison with the height but were not infantile when considered in comparison with the age. There was no real arachnodactyly. The weight ranged above the average not only for the age but, to a slight degree, for the size. The slender wrist indicated, however, a gracile type of skeleton. On the other hand, the well developed arm and calf indicated well developed musculature and fatty tissue.

On the basis of the anthropometric figures, the case may be considered an instance of incomplete arachnodactyly, or a forme fruste, with tallness of the body, slenderness of the skeleton, murmur of the heart and slight deformity of the auricles as partial symptoms. The picture was not absolutely typical, because of the well developed musculature and fatty tissue and the not very pronounced elongation of the fingers and toes.

CASE 6.—The patient, a boy 13 years and 6 months of age, had divergent alternating strabismus, severe iridodonesis and small pupils which responded poorly to atropine. Both lenses were dislocated downward and inward. In each eye the zonular fibers were stretched, of fanlike configuration and without pigmentation. The spaces between the stretched fibers were much wider than usual. There was a narrow temporal conus in each eye. The vision was 10/200 in the right eye, or 15/50 with a correction of +7.00 D. sph. $\bigcirc$ +1.50 D. cyl., axis 10, and 10/200 in the left eye, or 15/40 with a correction of +8.5 D. sph. $\bigcirc$ +1.25 D. cyl., axis 180.

From the anthropometric point of view the most striking features were the enormous elongation, especially of the hand and foot (table 2). Within these parts, the middle region of the hand was relatively more elongated than the fingers, and the same proportion held for the toes and the middle of the foot.

The musculature and the development of fatty tissue were remarkably poor. Contractures in the elbows, slight deviation in the form of the ears, kyphosco-

TABLE 1.—*Anthropometric Measurements in Case 5*

	Cm.	Inches	Normal for Age of: Years	Months	Deviation from Average for Real Age, Cm.	Deviation from Average for Real Size, Cm.
Height	118.0	46⅝	7	0	+14.0	.....
Sitting height	68.0	26⅝	8	4	+ 7.0	+ 2.0
Stem index	57.6%		5	10	—1.4%	+1.1%
Weight	22.8 Kg.	50 pounds	7	5	+5.8 Kg.	+0.8 Kg.
Circumference of:						
Head	52.0	20½	15 (?)	..	+ 3.2	+ 2.0
Chest	47.0	22½	5	6	+ 2.0	— 3.0
Wrist	12.6	5	6	6	+ 0.7	— 0.6
Forearm	17.5	7	8	10	+ 1.7	+ 1.0
Arm	17.4	7	8	8	+ 1.6	+ 0.9
Calf	23.5	9¼	7	9	+ 2.3	+ 0.5

Length of hand: 13.5 cm. (5¼ inches, or 13.3 cm.)
Relative length of hand: 11.4% (normal)
Breadth of hand: 5.9 cm. (2¼ inches, or 5.7 cm.)
Length of foot: 18.5 cm. (7¼ inches, or 18.4 cm.)

Fingers of the Right Hand:	First Phalanx, Cm.	Second Phalanx, Cm.	Third Phalanx, Cm.	Total Length, Cm.
1	0.6*	1.9	2.1	4.6
2	1.7	1.5	2.0	5.2
3	2.0	1.9	2.1	6.0
4	1.5	1.7	2.0	5.2
5	1.4	1.2	1.9	4.5

Toes of right foot	Total Length, Cm.
1	4.0
2	2.3
3	2.5
4	1.8
5	1.5

* Distance between two skin folds at base of thumb.

TABLE 2.—*Anthropometric Measurements in Case 6*

	Cm.	Inches	Normal for Age of	Deviation from Average for Real Age	Deviation from Average for Real Size
Height	177.0	69½	More than adult	+26.0 cm.	
Sitting height	90.0	35½	More than adult	+10.5 cm.	
Stem index	50.8%				
Weight	49.5 Kg.	108 lbs. 6 oz.	15 or 16	+7.5 Kg. (16½ lbs.)	—20 Kg. (—44 lbs.)

Circumference of:	Cm.	Normal for Age of	Deviation from Average for Real Age, Cm.
Head	61.0	More than adult	+8.0
Chest	74.5	14 years	+2.5
Inspiration	79.5		
Expiration	73.0		
Difference	6.5		
Wrist	16.5	16 years	+1.4
Forearm	21.0		
Arm	20.3	12¼ years	—1.2 (?)
Calf	26.5	10½ years	—3.2 (?)
Length of hand	22.1	More than adult	+6.0 (?)*
Breadth of hand	8.3		
Length of middle finger	9.6	More than adult	
Length of foot	29.5	More than adult	+4.5 (?)
Length of great toe	6.5	More than adult	
Length of head	22.0		
Breadth of head	16.5	Macrodolichocephaly	
Length-breadth index of head	75		
Span between extended finger tips	182		

* The average length of hand for an adult of the height of 177 cm. would be only 19.3 cm.

liosis, winged scapulas, pes planus and spur of the os calcis were present. The heart showed slight enlargement to the left, a brisk action and a short systolic murmur near the apex.

CASE 7.—The patient, a boy 13 years and 8 months of age, had vision of 5/200 in the right eye, or 20/40 with a correction of + 5.00 D. sph. ⊃ + 4.00

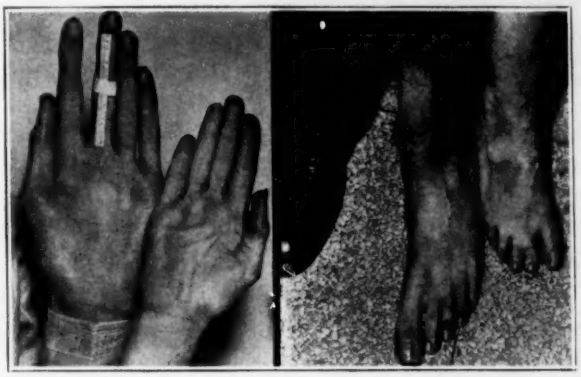

Fig. 5 (case 7).—The hands and feet of an arachnodactylic boy in comparison with those of a normal adult woman (5 feet 3 inches tall).

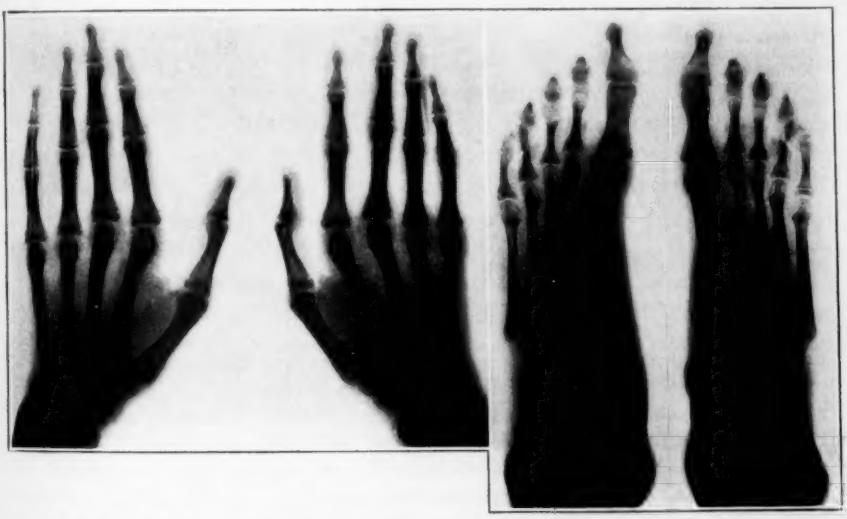

Fig. 6 (case 7).—Roentgenograms showing the extreme elongation of the fingers and toes.

D. cyl., axis 100, and of 5/200 in the left eye, or 20/40 with a correction of — 7.5 D. sph. ⊃ — 2.5 D. cyl., axis 150. The pupils were 3 mm. wide; after instillation of atropine the right pupil was 7 mm. and the left 6 mm. wide. There was severe iridodonesis in each eye. There was temporal dislocation of the right lens.

which was clear; correction was through the aphakic part of the pupil. The zonular fibers appeared to be stretched, grayish and without pigmentation. Behind the lens, deep in the vitreous, an aggregation of a large number of brownish gold, pinhead-sized pigment patches was seen with the slit lamp. The left lens was clear and only slightly dislocated upward and temporalward; correction was through the pupillary area containing the lens. The free margin of the lens showed a small coloboma. The fundi were normal.

The teeth and palate showed no characteristic symptoms. The lobuli of the ears were narrow and elongated but showed normal attachment; otherwise the ears were normal in shape. The spine exhibited typical high grade kyphosis with

TABLE 3.—*Anthropometric Measurements in Case 7*

	Cm.	Inches	Average for Patient's Age
Height	180.0	71	155.0 cm.
Sitting height	85.0	33½	81.0 cm.
Stem index	47.2%	..	52.0%
Weight	61.0 Kg.	134½ lbs.	45.0 Kg. for his height: 72.0 Kg.
Circumference of chest:			
Resting, absolute	86.0	34	76.0 cm.
Resting, relative	47.8%	..	48.2%
Inspiratory	89.0	35	
Expiratory	85.0	33½	
Difference	4.0		
Circumference of:			
Wrist	15.8	6½	15.4 cm.
Forearm	22.5	8½	21.8 cm.
Arm	23.5	9½	21.9 cm.
Calf	31.2	12¼	30.5 cm.
Length of right hand	20.2	8	17.3 cm.
Relative length of right hand	11.2%(?)	..	11.1%(?)
Breadth of right hand	8.0	3⅛	7.9 cm.
Breadth-length index	39.6%(?)	..	45.5%(?)
Circumference of head	58.5	23	53.0 cm.
Length of head	20.5	8	
Breadth of head	15.0	6	
Length-breadth index	73.0 (dolichocephaly)		

Fingers, mm.	1	2	3	4	5
First phalanx	7*	22	27	23	17
Second phalanx	25	25	30	28	21
Third phalanx	32	24	25	26	22
Whole finger	64	72	82	77	60
Length of foot	28.0				
Length of toes	55	42	38	35	38
Span between extended finger tips: 184 cm.					

* Distance between the two basic folds of the thumb.

moderate scoliosis of the thoracic part; the chest was deformed in accordance with the kyphoscoliosis. The heart was slightly deviated to the left by the disfigured chest wall; the first sound was slightly rumbling. The lungs were normal. The genital development corresponded to the age. The arches were rather flat.

The anthropometric measurements (table 3) showed the typical elongation of the long bones of the extremities and the typical narrow configuration of the hands. The low stem index was due to the deformity of the spine and the disproportionate growth of the bones of the legs. The length-breadth index of the hands was low, but the relative length of the hands was nevertheless closer to the average. The elongation of the metacarpal bones was particularly noticeable.

Of the 7 patients with arachnodactyly and dislocation of the lenses, 6 were male and 1 female. Investigation failed to reveal any hereditary transmission search in the immediate families yielding negative results.

The most remarkable from the point of view of the anthropometric findings was patient 5, a girl 4 years and 5 months of age who was 118 cm. tall, her height corresponding to that of a 7 year old child (14 cm. greater than the average for her age). Nevertheless, considering all the anthropometric data, one must conclude that she presented an incomplete picture of arachnodactyly. From the ophthalmologic standpoint, she showed a rare finding, unilateral dislocation of the lens, which has been reported only once, by Roch. (I do not consider the cases of Malbrán and Picoli, in which the unilateral dislocation occurred in microphthalmic eyes.) Roch's patient, a woman of 29, exhibited typical arachnodactyly: height 159 cm., span between the extended fingers 170 cm., length of the middle finger 13 cm. and length of the toe 10 cm. Kyphoscoliosis, patent foramen interventriculare, cyanosis and auricular flutter were noted, and dislocation of the lens was present only in the right eye.

The cases from the literature are summarized in table 4.

A statistical survey of the literature must take into consideration the fact that occasionally the same case was described by different authors, for example by Marfan and Méry and Babonneix, Pfaundler and Boerger, Thaden and Fleischer, Ormond and Williams and Cameron, Brock and Mueller and Rambar and Denenholz and Dvorak-Theobald. In the statistical data in the present paper, the cases of Euzière and Viallefont, Greyer, de Vicariis and Ceci, Morganti, Penido Burnier, Racugno, Kern and Schwartzweller were not included. The patient of the member of the Royal Medical Society of London and those of Bauer, Mader, Hamburger, Frontali, Benedict and Dollfus and Tetreau could not be considered because of the authors' failure to mention the sex.

Of the other 204 patients, 101 were male and 103 female. A hereditary or familial tendency was mentioned as positive in 58 cases and as questionable in 38 and was declared absent or was not mentioned in 113. Typical ocular symptoms (dislocation of the lenses or at least typical iridodonesis) were mentioned in 127 and ocular symptoms of questionable significance in 40 cases; ocular symptoms were absent or were not mentioned in 42 cases. Definite vitium cordis was present in 25 and other cardiac symptoms in 39 cases; cardiac symptoms were absent or were not mentioned in 45. Deformity of the ears was listed in 36 cases, and the hearing was defective in 6; the ears were normal or were not mentioned in 167.

A combination of symptoms involving the eyes, heart and ears was mentioned in 16 cases; a combination involving the eyes and heart with no mention of the ears, in 41.

While the number of female patients and the number of male patients were nearly equal for the whole group, with only a slight preponderance of the female patients, the proportion for ocular symptoms

TABLE 4.—*Statistical Survey of the Literature*

Author and Year	Age and Sex	Eyes	Heart	Ears	Skeleton	Heredity
Marfan 1896	5½ ♀	.....	.....	.....	Kyphoscoliosis; calcaneal spur; asymmetry of face and skull; contractures of tendons	Father, alcoholic addict; mother, migraine; 2 siblings died early; brother, congenital cataract; sister, strabismus
Achard 1902	18 ♀	.....	.....	.....	High patella	.....
Méry and Babonneix 1902	11½ ♀	Same case as that of Marfan (1896)		.....	Hyperextensibility of some of small joints	One sister, mother and mother's father, similar features; 2 other sisters normal
	11 ♀	Sister of last patient; forme fruste ?				
Poynton 1903	3 ♂	.....	.....	Large auricles; ridges of concha multiplied	Contractures in many joints; calcaneal spur; ligamentum patellae elongated; flatfoot	.....
Peritz 1911	18 ♀	Partial giantism restricted to distal parts of extremities, with dysgenitalism, infantile features, diseased thyroid gland (? goiter); questionable case				
Dubois 1912	10 ♀	.....	Vitium congenitale	.....	Congenital dislocation of hip; hammer toe	.....
Salle 1912	1½ ♂	Very narrow pupils shallow anterior chambers	Vitium congenitale	Large, flabby auricles	.....	Grandfather, alcohol addict; mother and mother's family, nervous
		Autopsy: patent foramen ovale, large sella with bony tumor				
Thomas 1914	1½ ♀	.....	.....	Deformity	Webbing of fingers; calcaneal spur	Father and father's father, nervous; mother's mother tall
Boerger 1914	..	1 case identical with Pfaundler's case				
Boerger 1914	9 ♂	Iridodonesis; myopic conus; remnants of pupillary membrane	Vitium congenitale	Large auricles	Winged and scaphoid scapulas; scoliosis; thorax paralyticus; calcaneal spur; genu recurvatum; pes planus	Father, alcoholic addict; diabetic, tall, strong; mother, gracile
Pfaundler 1914	1 ♀	Luxation of lenses; iridodonesis; hydrophthalmos	Vitium congenitale	Deformity	Kyphoscoliosis; funnel chest; flatfoot	.....
			Autopsy			
Calvo 1916	11 ♀	Dolichosténomélalgie acquired after birth with subacute illness; painful condition, probably with only superficially characteristic symptoms				
Neresheimer 1916	6 ♀	Partial color blindness; right side, remnants of persistent pupillary membrane	Dilated to left	Large	Asthenic type; pes planus; scaphoid scapulas; calcaneal spur	3 siblings died early; 1 sister had looked like her, gracile but normal grown; mother, gracile but not unusual, nervous, with struma
Rietschel 1917	9 mo. ♂	Unusual oblique position; lid fissure with high internal edge	.....	.....	Clubbed feet; calcaneal spur; scoliosis	.....

Lust 1919	1½ ♀	.....	.....	.....	Contractures in some finger joints, with some hyperextensibility	.....
Nobel 1920	14 ♀	.....	.....	.....	.....	.....
Rocher 1920	10 ♂	.....	.....	.....	Congenital dislocation of hips; prognathism; habitual dislocation of maxillary joint	.....
Thursfield 1920	.. ♂	.....	.....	Unusual form	Skull dolichocephalic, asymmetric; slight contractures, otherwise hyperextensibility; scoliosis; pigeon breast	.....
Dupérié, Dubourg and Guénard 1921	6 ♀	.....	.....	.....	Kyphosis; calcaneal spur; high palate; prognathism; congenital dilocation of hips	Parents, very young
Member of Medical Society of London, 1923	1 Sex not mentioned	Congenital dislocation of lens	?	.....	.....	.....
Poynton and Maurice 1923	16 ♀	.....	Hypertrophy and systolic murmur, dating from tonsillitis ?	.....	Tendency to flexion of all fingers; wrists unduly flexible; high palate; slight scoliosis	.....
Fowler 1924	9 ♂	Small pupils which did not dilate adequately; divergent strabismus	Loud systolic murmur	Large deficiency in cartilage	Scoliosis	.....
Fowler 1924	2½ ♀	Defective sight; dislocation of lenses; right, inward downward; left, downward	.....	Deformed	Calcaneus prolonged backward; slight contractures in elbows; slight genu recurvatum; slight undue mobility of some joints	.....
Ormond and Williams 1924	12 ♂	Luxation of lens	Functional systolic mumur ?	Deformity	High palate; dolichocephaly; winged scapulas; contractures in elbow joints; scoliosis	.....
Cameron 1924 and 1925	..	Same case as that of Ormond and Williams				
Egas Moniz 1926	11 ♀	.....	.....	.....	Dilated sella	.....
Piper and Irvine-Jones 1926	1¾ ♀	Luxation of lens	Vitium congenitale Autopsy	.....	Cleft palate; kyphosis; webbing; brachycephaly	Parents, young
Schlack 1926	5 ♂	Luxation of lens Nervous symptoms similar to those of Friedreich's syndrome	Vitium	Deformity	Kyphosis; funnel-shaped chest; calcaneal spur	.....
Thomas 1926	2½ ♀	.....	.....	Deformity	Webbing; flatfoot; calcaneal spur	Mother, neuropathic

TABLE 4.—*Statistical Survey of the Literature—Continued*

Author and Year	Age and Sex	Eyes	Heart	Ears	Skeleton	Heredity
Baessler and Schneider 1927	18 ♀	.....	Murmur; arrhythmia; cyanosis; rather vegetative; neurotic	.....	Unusual motility in various joints	Mother, asthenic but not unusually so
Bauer 1927	..	.....	.....	Deformity	.....	.....
Brock 1927	10 ♀	.....	.....	.....	Scoliosis; high palate; habitual luxation of mandibula and radius; spina bifida occulta; contractures in finger joints; flatfoot; hammer toe; calcaneal spur	.....
Ganther 1927	6½ ♀	No eyelashes; deep physiologic excavation; pale optic nerve	.....	Hearing defect	Kyphoscoliosis	.....
Grosser and Igersheimer 1927	♀ Age not mentioned	Luxation of lens; slight megalocornea	.....	.....	.....	.....
Mader 1927	7 Sex not mentioned	.....	.....	.....	.....	.....
Moro 1927	12 ♀	..... Condition similar to	Vitium congenitale Friedreich's syndrome	.....	Calcaneal spur; atrophic ribs on right; reflexes increased	.....
Rominger 1927	6½ ♀	Deeply set; nystagmus; convergent strabismus	.....	.....	Kyphoscoliosis	.....
Zuber 1927	1 ♀	Nystagmus; convergent strabismus	.....	.....	Cleft palate; flatfoot; calcaneal spur	.....
Bier 1928	7 ♀	Luxdtion of lens	Vitium	.....	Kyphoscoliosis; webbing, pes planus and valgus	Father and father's father, similar habitus
Fleischer 1928	1½ ♂	Luxation of lens; megalocornea; right, dislocation into chamber; left lens small, ⅔ diameter of cornea	.....	Large, lobuli	Calcaneal spur	Father and father's sisters and brothers reported as having thin arms and legs but stout trunk
Hamburger 1928	5 wk. ♀	.....	.....	.....	Small sella	.....
Kallius 1928	6 mo. ♂	.....	.....	Deformity	Contractures; pes valgus	.....
Schreiber, Duhem and Jubert 1928	6 mo. ♀	.....	.....	.....	Hypermotility in various joints; kyphosis; large sella	.....

Zuber and Cotenot..... 1928	5 ♀	Strabismus	.....	Deformity	Pes planus; calcaneal spur; small sella; spina bifida occulta	.....
Brock..... 1929	11½ ♀	Cataract on both sides; mikrophthalmos on left; degeneration of macula	.....	Hearing defect	Kyphosis; lordosis	.....
Carrau..... 1929	3 ♀	..... Mental backwardness	.....	.....	Kyphoscoliosis; congenital dislocation of hips and subluxation of knee joints; pes equinus; brachycephaly; funnel-shaped chest	.....
Frontali..... 1929	7½	.....	.....	.....	Supernumerary osseous centers in phalanges	Parents related; 3 siblings, similar features; symptoms also in family of father and mother
Mueller..... 1929	16 ♀	Deeply set	.....	.....	Funnel-shaped chest; scoliosis; flatfoot	.....
	15 ♀	.....	.....	.....	Funnel-shaped chest; kyphosis; deformity of ribs	.....
	4 ♂	Luxation of lens	.....	Deformity	.....	.....
	6 ♀	.....	.....	.....	Crus valgum; funnel-shaped chest; scoliosis; deformity of ribs	.....
Ormond..... 1929	17 ♀	Dislocation of lens	Vitium	.....	Kyphoscoliosis	.....
Schrader..... 1930	18 ♂	Deeply set	.....	Large lobules	Pes planus and valgus; contractures of toes; funnel-shaped chest	Incest; mother was daughter of father
Thaden..... 1929	..	Same case as that of Fleischer (1929) Right, high myopia; corneas, 13 and 12.5 mm., respectively		.....	.....	.....
Wagner..... 1929	6 ♂	.....	.....	Deformity	Small sella; contractures (Dupuytren's)	.....
Young..... 1929	14 ♀	Amyotonia	.....	.....	Clubbed feet; small sella	.....
	3 ♀	Amyotonia Patient died of pneumonia	Large lobules	Large lobules	Highly arched, narrow palate; contractures in arms and legs; pigeon breast; lumbar kyphosis	.....
	5½ ♀	Dislocation of lenses; high myopia	.....	Large and deformed	Os calcis spurred; pes planus; highly arched palate; sella elongated but small; kyphosis	Sister of next patient; mother, dislocation of lenses and a similar aspect
	7½ ♂	Dislocation of lenses	.....	.....	Slight kyphosis; os calcis spurred; patello extremely high; funnel-shaped chest	Brother of last patient; third and fourth children
de Haas..... 1930	7 ♂	Ectopia of lens	.....	.....	.....	Brother of next patient
	10 ♀	Ectopia of lens	.....	.....	.....	Sister of last patient; father, long hands and feet

TABLE 4.—*Statistical Survey of the Literature—Continued*

Author and Year	Age and Sex	Eyes	Heart	Ears	Skeleton	Heredity
Zuber 1930	7 mo. ♀	?		Deformed	Atresia of lower jaw with glossoptosis; thorax deformed; os calcis spurred	
Albanese 1931	13 ♀				Pes valgus	
Ellis 1931	8 ♀	Ectopia of lenses; iridodonesis; blue scleras; small patch of choroidoretinitis in outer part of left fundus				Blue scleras inherited through mother, arachnodactyly through father
Ingram and Inglis 1931	2½ ♀		Congenital heart disease	No lobules	Deformity of feet and toes; arched palate; laxity of ligaments and muscular hypotonia	Absence of lobules of the ears in 3 other siblings
Nicolo 1931	8 ♂	Iridodonesis; remnants of pupillary membrane; dislocation of lenses upward, outward	Forme fruste (gracile longilineal, good nutrition)			
Vogt 1931	13 ♂	Dislocation of lenses	Vitium		Kyphoscoliosis; os calcis spurred	
Weve 1931	40 ♂	Dislocation of lenses; vitreous atrophic; irises discolored	Vitium ?	Large lobules	Slight kyphoscoliosis; high narrow palate	Grandfather reporrted to have been similar; father of next 3 patients
	15 ♂	Congenital dislocation of lenses			Slight kyphoscoliosis; thorax deformed; high palate; irregularities in position of teeth	Son of last patient; brother of next 2 patients
	12 ♂	Congenital dislocation of lenses	Murmur	Defect of lobules	Malposition of teeth; high narrow palate; slight scoliosis; deformed thorax; hammer toe; slightly spurred os calcis	Brother of last patient
	9 ♀	Lenses small, subluxated; iridodonesis; lenses maximally curved; dislocated nasalward			Progressive deformities of thorax and spine; high palate; malposition of teeth	Sister of last patient
	16 ♂	Subluxation of lenses	Murmur		High, narrow palate; malposition of teeth; elongated ligamentum patellae	Forme fruste in grandfather, uncle and cousin; see next case
	? ♂	Forme fruste	?	Large	Scoliosis	Grandfather of last patient
	62 ♂	Forme fruste			Pes planus; kyphoscoliosis	Son of last patient, 7 children but only 1 son similar (next patient)

	24 ♂	Forme fruste	.....	.....	Kyphosis; high palate	Son of last patient
	16 ♀	Congenital dislocation of lenses	.....	.....	.....	Probably similar type of condition in mother and in 7 of 10 siblings, but only slight features
	4½ ♂	Large; deeply set	Murmur	Large	Winged scapulas; pigeon breast; genu recurvatum	.....
	48 ♂	Congenital dislocation of lenses	.....	.....	High palate; pes planus	Had 16 children; of 5 who died, 4 reported as of arachnodactylic habitus; of 11 living, 3 showed arachnodactyly and dislocated lenses (the next 3 patients)
	19 ♂	Congenital dislocation of lenses	.....	.....	Winged scapulas; narrow chest	Son of last patient
	18 ♂	Congenital dislocation of lenses	.....	.....	.....	Brother of last patient
	16 ♀	Congenital dislocation of lenses	Vitium ?	.....	Scoliosis	Sister of the last 2 patients
	9 ♀	Congenital dislocation of lenses	Cases identical with the 2 cases of de Haas	.....	.....	Brother of next patient; father probably had similar condition
	6 ♂	Congenital dislocation of lenses		.....	.....	Brother of last patient; father probably had similar condition
Abelsdorff..... 1932	16 ♀	Dislocation of lenses	.....	.....	Kyphoscoliosis	8 siblings, only 1 of them a similar type, but no pathologic symptoms
Custodis..... 1932	Adult ♂	Dislocation of lens	.....	.....	.....	Father
	? ♂	Dislocation of lens	.....	.....	.....	Son
Dor..... 1932	Adult ♂	Dislocation of lenses	.....	.....	.....	.....
Dvorak..... 1932	24 ♀	Dislocation of lenses; iridodonesis; small pupils; myopia, —18.00 D.	Old chronic pericarditis, adhesive ?	.....	Clubbed feet; highly arched palate	.....
Franceschetti..... 1932	28 ♀	Coloboma of lenses; right conus, myopic; right, —35.00 D. sph.; left, —13.00 D. sph. ⊂ —3.00 D. cyl.; right conus ⅓ disk wide; not only lenticular but degenerative stigma	.....	.....	.....	Father, unusually long narrow hands
Hudson..... 1932	19 ♂	Congenital dislocation of lenses	.....	.....	Deformity of chest	3 siblings of 8 had peculiarities similar to those of patient
		Supposed to have been normal until 6th or 7th year of life; atypical case				

TABLE 4.—*Statistical Survey of the Literature—Continued*

Author and Year	Age and Sex	Eyes	Heart	Ears	Skeleton	Heredity
Killmann..... 1932 and 1934	29 ♂	Congenital dislocation of lenses into vitreous divergent strabismus	.....	.....	Kyphoscoliosis; pes planus; narrow, highly arched palate	Father reported to have had vitium cordis and similar type of bodily structure; father of next patient
	2½ ♂	Dislocation of lenses downward, nasalward	..... Questionable case	.....	.....	Son of last patient
	36 ♀	Subluxation of lenses upward, outward; lenses small and globular	..... Questionable case	.....	.....	Father, similar type of bodily structure and vitium cordis (?); mother of next patient
	16 ♀	Subluxation of lenses upward, outward; iridodonesis	.....	.....	Pes planus; highly arched palate	Daughter of last patient
	6 ♂	Luxation of lenses outward, upward	.....	.....	Winger scapulas; highly arched palate	Father, forme fruste ?
	36 ♂	Myopia; slightly myopic conus	..... Forme fruste: only large hands and feet	.....	.....	Father of last patient
	31 ♂	Luxation of lens; right, upward, nasalward; left, into vitreous; strabismus	Murmur	.....	Scoliosis; high palate; slight contractures of fingers	.....
	11 ♂	Subluxation of lens downward; globular lens	Vitium	.....	Scoliosis; high palate; round skull	3 brothers died early; 2 sisters, questionable ocular conditions
Padovani..... 1932	20 ♂	Dislocation of lenses; left sclera blue; right, leukoma of cornea after ulcer	.....	.....	.....	.....
Pentagna..... 1932	11 ♂	Slight exophthalmos; hypermetropia, +2.00 D. Congenital syphilis; acromegalia ?; not typical	.....	.....	.....	.....
Sorsby..... 1932	16 ♀	Subluxation of lenses	..... Typical arachnodactyly	.....	.....	.....
Weill.....1 1932	42 ♀	.....	..... Forme fruste	.....	Short; mild scoliosis; tendinous retractions	.....
2	46 ♂	Ectopic lenses	Old endocarditis	.....	Prognathism; dolichocephaly; coxa valga; tendinous retractions; intracranial ossifications	.....
		Autopsy: partial defect of falx cerebri with concrescence of frontal lobes				
3	27 ♀	Ectopic lenses Autopsy: old endocarditis	Dilatation; hypertension	.....	Flat chest; hallux valgus; flatfoot, genu valgum; scoliosis; osteosclerosis of skull	.....
4	52	Coloboma of irises	.....	.....	Scoliosis	Mother of "patient 6"

	4	52 ♀	Coloboma of irises and lenses; iridodonesis	.....	.....	Scoliosis	.....
	5	36 ♀	Iridodonesis; subluxation of lenses	.....	.....	Flat chest; flatfoot; scoliosis; hallux valgus	Mother of "patient 6"
	6	6 ♂	Dislocation of lenses	.....	.....	Spina bifida; coxa valga	Son of "patient 5"
	7	38 ♀	Dislocation of lenses with calcification	.....	.....	Dwarfish; flatfoot	Mother of "patient 8"
	8	3 ♂	Dislocation of lenses	.....	.....	Spina bifida	Son of "patient 7"
				Forme fruste of arachnodactyly ?			
Patterson..... 1933		11 ♀	Prominent, but no other pathologic findings	.....	.....	Highly arched palate; upper jaw protruded; pigeon breast; winged scapulas; increased mobility in shoulders, elbows, forearms and hands; slight scoliosis and kyphosis; flatfoot	.....
Weber..... 1933		19 ♂	Congenital dislocation of lenses	Inclination to venous thrombosis; dilated superficial veins	.....	Pigeon breast; scoliosis	Brother of next patient
		15 ♀	Congenital subluxation of lenses; iridodonesis; extreme myopia	.....	.....	Scoliosis; lordosis; funnel chest	Sister of last patient; youngest of 14 siblings; 6 dead, 6 normal
Amsler..... 1934		..	Upward dislocation of lenses in 7 persons (3 generations) of 1 family; most of them tall and slender; probably formes fustes of arachnodactyly				
Coppez..... 1934		17 ♀	Subluxation of lenses	.....	.....	.....	.....
				Arachnodactyly			
Fast..... 1934		40 ♂	Subluxation of lenses	.....	.....	Scoliosis	Father, long extremities
King..... 1934		37 ♀	Iridodonesis; ectopia of lenses, upward, inward; delicate opacities of vitreous; chorioideal scars below disk; diffuse haze throughout lenses	.....	.....	.....	Mother of next 2 patients
				Forme fruste of arachnodactyly ?			
		18 ♀	Ectopia of lenses upward; coloboma of lenses with local opacities	.....	.....	.....	Daughter of last patient
		13 ♀	Ectopia of lenses; right, lateral; left, upward, outward; coloboma of lenses; left, pupillary membrane; old central chorioiditis, right and left	.....	.....	.....	Sister of last patient; another older sister normal
				Rather typical arachnodactyly			

TABLE 4.—*Statistical Survey of the Literature—Continued*

Author and Year	Age and Sex	Eyes	Heart	Ears	Skeleton	Heredity
Kurz 1934	25 ♀	Luxation of lens	.....	.....	Kyphoscoliosis; pes planus	Father of similar type ?
	2½ ♀	Luxation of lens; status dysraphicus	Vitium ?	.....	Gibbus; funnel-shaped chest; pes planus and cavus	Father of similar type
	34 ♀	Ectopia of lens; syphilitic changes	.....	.....	Scoliosis	.....
Viallefont and Temple 1934	..	Luxation of lenses	.....	.....	Kyphosis	Father and 3 of his 5 children, same syndrome
	Compare: Villard, Viallefont and Temple (1934)					
Villard, Viallefont and Temple 1934	11 ♂	Dislocation of lenses upward, backward	Sounds unclear	.....	.....	Father, dislocation of lenses; brother of next patient; 1 sister, dislocation of lenses but no arachnodactyly; mother and 2 other siblings, normal
				Typical aspect		
	9 ♀	Dislocation of lenses upward, backward	Sounds unclear	.....	Scoliosis	Sister of last patient
Bakker 1935	16 ♂	Congenital dislocation of lenses	Only anatomic description of the extirpated lenses			
	19 ♀	Congenital dislocation of lenses	.....	.....	.....	.....
Becker 1935	61 ♀	Dislocation of lens; right, upward, outward, posterior, with cataract; left, clear	Vitium	.....	Pes planus	1 normal son; the 2 other sons and 3 grandchildren are next patients
	34 ♂	Ectopia ?	.....	.....	.....	Son of last patient
			Forme fruste			
	4 ♂	Dislocation of lens inward, upward; myopia, —12.00 D.	.....	.....	.....	Brother of last patient
			Forme fruste			
	35 ♀	Normal	.....	.....	.....	Brother of last patient
			Only reminding one in habitus of patient similar types			
	9 ♂	Dislocation of lens upward, inward	.....	.....	.....	Son of last patient
			No arachnodactyly, patient of similar type			
	8* ♂	Ectopia of lens	.....	.....	.....	One of twins; brother of last patient
			Forme fruste			
	8* ♂	Ectopia of lens inward, upward	.....	.....	.....	One of twins; brother of last patient; 3 other siblings normal (1 with hammer toe and rheumatic heart, another with flatfoot)
			Forme fruste			

Buecklers 1935	8 ♂	Subluxated globular lenses; aplasia of zonula	.....	Hearing defect	Scoliosis; high, narrow palate; aplasia and anomalies of teeth Pectus carinatum	.....

Buscklers..... 1935	8 ♂	Subluxated globular lenses; aplasia of zonula	.....	Hearing defect	Scoliosis; high, narrow palate; aplasia and anomalies of teeth	.....
	20 ♂	Subluxation; iridodonesis; globular lens	First sound unclear; drop heart	.....	Pectus carinatum	.....
	12 ♂	Dislocation of lenses	.....	.....	.....	A sister reported with same anomaly
Christophersen..... 1935	9 mo. ♂	Deeply set; myopia ?	.....	.....	.....	Similar types in mother's family
François..... 1935	12 ♂	Dislocation of lenses	Unusual shape in roentgenograms	.....	Deformed thorax; scoliosis; winged scapulas; malposition of teeth	Mother, possibly forme fruste
Isnel and Hakami..... 1935	27 ♂	Dislocation of lenses; glaucoma on left; microcornea; myopia; chorioretinal changes	.....	.....	.....	.....
Lloyd..... 1935	5 ♂	Dislocation of lenses outward, upward	.....	.....	.....	4 of 6 siblings affected, mother and mother's father, similar type of skeleton but no ocular symptoms
	9 ♂	Dislocation of lenses		.....	.....	.....
	13 ♀	Dislocation of lenses		.....	.....	.....
	18 ♀	Dislocation of lenses		.....	.....	.....
Morard..... 1935	10 ♂	Ectopia of lenses	Murmur and frémissement	.....	Kyphosis; thorax deformed; hyperlax ligaments	.....
Passow..... 1935	14 ♀	Dislocation of lenses; heterochromia of irises	.....	.....	Scoliosis; high palate	.....
	20 ♂	Luxation of lens	Vitium	.....	.....	.....
Puglisi-Duranti..... 1935	12 ♀	Macular coloboma of left eye	Systolic murmur; accentuated second sound at pulmonary valve	.....	Pes valgus	Syphilis in family
				Forme fruste		
Tikhomirov..... 1935	16 ♂	Dislocation of right lens downward, of left downward, outward	.....	.....	Height, 185.5 cm.	.....
	23 ♂	.....	.....	.....	Height, 178.7 cm.; weight, 64.5 Kg.	Tall persons in family; 2 siblings with corectopia
	27 ♂	Dislocation of right lens upward, inward, of left upward, backward; myopia, —4.5 D.; posterior staphyloma each eye; detachment of retina on left	.....	.....	Height, 178.5 cm.; weight, 65.0 Kg.	.....

* Twins.

TABLE 4.—*Statistical Survey of the Literature—Continued*

Author and Year	Age and Sex	Eyes	Heart	Ears	Skeleton	Heredity
Benedict 1936	7 wk. Sex not mentioned	.....	.....	.....	Contractures of several fingers	.....
Burch 1936	8	Dislocation of lenses downward. outward; lenses opaque	Systolic murmur; enlarged borders	.....	Funnel-shaped chest; spinal deformity	.....
	10 ♂	Dislocation of lenses	Serious cardiac involvement	.....	High, narrow, arched palate	.....
	12 ♂	Dislocation of lenses upward, backward; lenses opaque	Drop heart	.....	Mild scoliosis	.....
	25 ♀	Dislocation of lenses upward, backward	Systolic murmur	.....	Slight scoliosis	.....
	8 ♂	Dislocation of lenses upward	.....	.....	Weak joints; narrow, elongated fingers and toes	Father, 1 brother and 1 sister, ectopic lenses; somewhat arachnodactylic features; sister, systolic murmur
	15 ♂	Dislocation of lenses downward, temporalward	Diastolic murmur	.....	Pes valgus; spinal curvature	Paternal grandmother died of cardiac disease, had long bones; 1 brother died of cardiac disease; 1 sister of pneumonia; another sister and the father are the next patients
	50 ♂	Dislocation of lenses; upward; opacities	Systolic murmur at bases and diastolic murmur at aortic region	.....	Funnel-shaped chest	Father of last patient and of next patient
	21 ♀	Dislocation of lenses upward, nasalward	.....	.....	Funnel-shaped chest	Daughter of last patient and sister of patient before last
Calogero 1936	14 ♂	Dislocation of lenses; atrophy of irises; persistent pupillary membrane	Pericarditis ? accentuated tone at pulmonary valve	.....	Typical arachnodactyly	.....
	13 ♀	Iridodonesis; ectopic of pupilla	.....	.....	Slight deviation of spine	.....
Curschmann 1936	51 ♂	Hyperopia; astigmatism	Forme fruste of arachnodactyly	.....	Funnel-shaped chest	Father of next 2 patients
	21 ♂	Dislocation of lenses	.....	.....	Funnel-shaped chest	Son of last patient
	16 ♀	Iridodonesis	.....	.....	Funnel-shaped chest	Sister of last patient

Delord and Viallefont 1936	15 ♂	Dislocation of lenses	..... Genital hypoplasia	.....	Scoliosis; legs and feet deformed similarly to those in Friedreich's syndrome	Son of next patient
	41 ♂	Congenital dislocation of lenses	.....	.....	.....	Father of last patient
Kurz 1936	34 ♀	Dislocation of lenses	Syphilitic infection	.....	Scoliosis; hammer toe	.....
Lodi 1936	6 ♂	Deeply set; miotic pupils	Murmur at basis	Large auricles irregularly shaped	Kyphoscoliosis; costa fluctuans decima	Mother, tall, slender, but not excessively so; pleurisy; arthritic rheumatism
Schilling 1936	14 ♂	Bilateral dislocation of lens, temporal conus and pigment deposit in macula, besides generally poor pigmentation	Systolic murmur	Large ears; hard of hearing right ear	Scoliosis; winged scapulas; narrow jaws; flat chest	.....
			Striae distensae; ataxia like that in Friedreich's syndrome			
Westendorf 1936	11 ♀	Eyeglasses, but no special pathologic findings	.....	Unusually shaped auricles	Scaphoid scapulas; funnel-shaped chest; slight scoliosis	.....
	5½ ♀	Deeply set; neurologic symptoms	.....	Large; lobular	Kyphoscoliosis	.....
	3½ ♀	Deeply set	Systolic murmur	Large; lobular	Kyphosis; funnel-shaped chest	.....
Charamis 1937	5½ and 9½ ♀	Dislocation of lenses; cataract; heterochromia of iris; large bulbi; pupillary membrane	Systolic murmur; arterial hypertension	.....	Kyphoscoliosis; flat chest	.....
Chiari 1937	1 ♀	.....	.....	.....	Kyphosis	.....
Fischbach 1937	1½ ♂	Normal	Vitium congenitale	Deformed	Scoliosis; luxation of hips and of right patella; pes valgus; torticollis	Formes frustes in father's and in mother's family ?
	14 ♀	Luxation of lens; left, myopic conus; right, ablatio retinae	.....	.....	Scoliosis; pes planus and valgus	Father and father's sister of similar type
	7 ♂	Luxation of lens	.....	.....	.....	.....
Goedl 1937	44 ♀	Remnants of pupillary membrane; right, high myopia; perinuclear opacities; coloboma of iris nasalward and downward, of lens and of chorioid, bilateral	Vitium cordis mitrale	.....	Deformities of spine and extremities	Father and 2 of 11 siblings might have had incomplete forms of arachnodactyly

TABLE 4.—*Statistical Survey of the Literature—Continued*

Author and Year	Age and Sex	Eyes	Heart	Ears	Skeleton	Heredity
Huber, Florand and Lièvre.... 1937	11 ♂	Ectopic lenses; iridodonesis	Systolic murmur	.....	Flat chest	Mother, highly arched palate; father's sister, unusually tall
Huber, Florand and Lièvre.... 1937	11 ♂	Ectopic lenses;	Systolic murmur	.....	Kyphosis	.....
Lloyd..... 1937	15 ♂	Small corneas; left and probably right lens dislocated; pupils did not dilate; opacities in lenses; remnants of pupillary membrane, both sides	Pulmonary stenosis	.....	Lordosis; sternum depressed; little fingers curved	Father, tall and thin, uncle of the mother
	7 ♂	Lenses small, not clear, margins eccentric; lenses tremulous; some months later, right lens dislocated into anterior chamber; later, other lens dislocated	.....	..... Mental deficiency ?	.....	Father, congenital ptosis of left upper lid
	9½ ♀	Dislocation of lenses	.....	.....	.....	9 month old sibling, large feet; mother, lenses dislocated, but short and plump (transmitter, with incomplete syndome)
	7½ ♀	Dislocation of lenses	First pulmonary sound rough	Deaf from birth without pathologic findings	Typical arachnodactyly	Sister of next patient; daughter and grand-daughter of 2 following patients
	? ♀	Poor vision (Killed at early age in accident)	.....	Deaf	Thin bones	Sister of last patient
	Adult ♂	Dislocation of lenses; opacities	.....	.....	Typical arachnodactyly	Father of 2 last patients
	Adult ♂	Poor vision Habitus as in arachnodactyly	.....	.....	.....	Father of last patient
	14 ♂	Dislocation of lenses	.....	.....	.....	Father and grandfather, poor eyes
Malbrán and Picoli..... 1937	♀	Dislocation of lenses Syphilis and arachnodactyly	Aortitis	.....	.....	1 brother, dislocation of lenses; father and 2 of his brothers, of similar type; sister of next patient
	♀	Dislocation of lenses Syphilis and arachnodactyly	Aortitis	.....	.....	.....
	3 ♀	Microphthalmia; dislocation of one lens	Aortitis	.....	.....	3 sisters with syphilis, arachnodactyly, displacement of lenses and microphthalmia

Pino, Cooper and Van Wien... 1937	6 ♂	Poor vision	.....	.....	Webbing of fingers; poor development of muscles; mild kyphoscoliosis; highly arched palate	.....
Roch..... 1937	29 ♀	Dislocation of lens of right eye	Open foramen ovale	.....	Kyphoscoliosis	.....
Roederer..... 1937	14 ♂	Myopia	.....	.....	Scoliosis; kyphosis; flat chest	.....
Schwarzweller..... 1937	..	7 patients, 2 uniovular twins		.....	.....	.....
Apert..... 1938	13 ♀	Anisocoria	Open duct of Botalli; atheroma of pulmonary artery	.....	Thorax deformed; genu valgum	.....
Benoit..... 1938	15 ♂	High myopia and bilateral dislocation of lenses	.....	.....	Typical skeletal changes	.....
Buecklers..... 1938	..	Several cases of ectopia lentis with arachnodactyly within one family; no details on single cases				
Cockayne..... 1938	6 ♂	Iridodonesis; miosis	Systolic thrill and murmur	Large; prominent	.....	.....
Dracondaidis..... 1938	25 ♀	Luxation of right lens into anterior chamber, of left into vitreous	.....	.....	Height, 187 cm.; giantism; distention of sella	Few members of family showed giantism; mother, congenital coloboma of iris and macular changes, right
Futcher and Southworth..... 1938	12 ♂	Slight refractive error	Mitral insufficiency; rheumatic polyarthritis	Projecting	Scoliosis; slight webbing of fingers and toes	Mother, long fingers and toes and hunched back
	13 ♀	.....	.....	Prominent	Pigeon breast; scoliosis	A first cousin, unusually long fingers, rheumatic fever
Giraud, Bocca, Jayle and Moekers, 1938	9 mo. ♀	Iridodonesis; miosis; microcornea; myopia	Systolic murmur; interventricular opening	.....	.....	.....
van der Hoeve..... 1938	16 ♂	Ectopia of pupils and coloboma of lenses	.....	.....	.....	.....
Laval..... 1938	50 ♂	Dislocation of lenses; iridodonesis	.....	.....	Kyphosis; asymmetric legs	.....
	10 ♀	Dislocation of lenses; ididodonesis	.....	.....	Lordosis; highly arched palate	.....
Nobécourt, Cathala and Temerson, 1938	2	Dislocation of lenses; coloboma of left iris; aniridia on right; chorioretinal lesions	..... Small and underweight; brachycephalic;	.....	..... forme fruste ?	.....
Roederer..... 1938	13 ♀	Strabismus; small pupils	Tachycardia	.....	Coxa valga; flat chest; kyphosis; scoliosis	.....
Semah..... 1938	11 ♀	Blue scleras	.....	.....	Deformed thorax; fragilitas ossium	.....

TABLE 4.—*Statistical Survey of the Literature—Continued*

Author and Year	Age and Sex	Eyes	Heart	Ears	Skeleton	Heredity
Dollfus and Tetreau..... 1939	16 Sex not mentioned	Luxation of lenses upward, backward; myopia, —4.50 D.; fundi normal	.....	.....	.....	.....
Fleischer..... 1939	..	9 cases of archnodactyly with ectopia of lens; no details on single cases				
Moore..... 1939	6 ♂	Iridodonesis; miosis; atrophy of dilator fibers; myopia, —38.00 D.	Congenital heart disease	.....	.....	.....
Passow and Roemmelt..... 1939	..	Mother and 4 children had ectopic lenses, typical arachnodactyly, deformities of spine, webbing of fingers, highly arched palate; 1 child normal				
		2 other patients with similar conditions; no details				
Rambar and Denenholz..... 1939	2 ♂	Dislocation of lenses; iridodonesis; axial myopia; defective dilator or pupillae muscle; accessory oblique muscle	..... Autopsy	.....	.....	.....
de Saint-Martin..... 1939	28 ♀	Luxation of 1 lens into anterior chamber, of other into vitreous; small lens; atrophy of iris	Slight tachycardia	.....	Height, 158 cm.; span, 162 cm.; scoliosis; lengthening of skeleton of upper extremities only; dolichocephaly; difference in size of breasts	Family not examined for possible hereditary changes
Schmieding..... 1939	7 ♀	Remnants of pupillary membrane; nystagmus to left	.....	Large; protruding	Pes planus; dilocation of hips	Brother of next patient
	5 ♂	Remnants of pupillary membrane; fixation nystagmus	.....	.....	Pes planus; dislocation of hips	Sister of last patient
Stewart..... 1939	16 ♂	Miosis; corectopia; nystagmus	..... Mental defect; epileptic attacks	.....	Deformities and contractures	.....
Stieren..... 1939	35 ♀	Dislocation of lenses upward, inward	.....	.....	.....	.....
Villani..... 1939	15 ♀	Asymmetric dislocation of lenses	.....	.....	.....	2 other children normal; mother suffering from same condition

was very different. Among 77 male patients with typical arachnodactyly, 63 had typical and 3 had other ocular symptoms, while only 7 had no ocular symptoms. Among 91 female patients with typical

TABLE 5.—*Statistics on 204 Cases of Arachnodactyly*

Presence of Ocular Symptoms

	Male			Female		
	Dislocation of Lenses or Iridodonesis	Other Ocular Symptoms	No Ocular Symptoms	Dislocation of Lenses or Iridodonesis	Other Ocular Symptoms	No Ocular Symptoms
Typical cases	63	13	7	47	21	21
Atypical cases, or cases of formes frustes	10	3	4	4	2	6
All cases	73	16	11	53	23	27

Presence of Cardiac Symptoms

	Male			Female		
	Vitium Cordis	Murmur or Other Minor Symptoms	No Cardiac Symptoms	Vitium Cordis	Murmur or Other Minor Symptoms	No Cardiac Symptoms
Typical cases	12	20	51	13	19	60
Atypical cases, or cases of formes frustes	0	0	17	0	1	11
All cases	12	20	68	13	20	71

Heredity

	Male			Female		
	Positive	Questionable	Negative	Positive	Questionable	Negative
Typical cases	14	16	42	22	17	53
Atypical cases, or cases of formes frustes	11	3	3	2	2	8
All cases	35	19	45	24	19	61

Presence of Anomalies of Ears

Male			Female		
Deformity of Ears	Hearing Defect	Ears Normal or Not Mentioned	Deformity of Ears	Hearing Defect	Ears Normal or Not Mentioned
21	2	78	14	4	86

Combination of Ocular and Cardiac Symptoms

	Male	Female	Total
Combined with anomalies of ears	12	4	16
Without anomalies of ears	17	24	41
All patients	**29**	**28**	**57**
Total number of patients	101	103	204

arachnodactyly, only 49 had typical and 31 had other ocular symptoms, while 21 had no ocular symptoms. Still more striking is the relation when one considers the patients with atypical or abortive symptoms of arachnodactyly. Of 17 male patients, 10 had typical and 3

had other ocular symptoms, but only 4 had no ocular symptoms; while of 12 female patients with abortive or questionable arachnodactyly, only 4 had typical and only 2 had other ocular symptoms and 6 had no ocular symptoms.

No such difference was observed, however, in the sex distribution with regard to the cardiac symptoms. Of the patients with typical arachnodactyly, 12 male and 13 female patients had vitium cordis, 20 male and 18 female patients had other cardiac symptoms and 52 male and 61 female patients had no disease of the heart. Of the patients with formes frustes, only 1 female patient had a questionable cardiac symptom. With regard to all the other patients the findings were negative or the condition of the heart was not mentioned.

Heredity was a more frequent factor among the male than among the female patients, and, again, the relation was more striking among those with an abortive or questionable form than among those with the typical syndrome. Of 83 typically arachnodactylic male patients, 24 showed a positive and 15 a questionable heredity, but of 91 female patients typically arachnodactylic, 22 had a positive and 17 a questionable heredity. Among the patients with typical or questionable arachnodactyly, 11 male patients had a positive heredity and 3 had a questionable heredity but only 3 had no hereditary strain, while only 2 female patients had a positive and 2 a questionable heredity, as against 18 without a hereditary factor.

The combination of ocular and cardiac symptoms was but slightly more frequent in the male than in the female patients—affecting 29 of 100 male and 28 of 103 female patients—but it is interesting to note that this relation changes as soon as one differentiates between the patients who had aural symptoms in addition to the ocular and cardiac symptoms. For the complete syndrome, comprising ocular, aural and cardiac symptoms, the proportion was 12 male to 4 female patients, while for ocular symptoms combined with cardiac symptoms but without pathologic changes in the ears there were 17 male and 24 female patients.

Deformities of the ears were found in 21 male but in only 14 female patients; defective hearing, in 2 male but in 4 female patients, and no pathologic changes in the ears, in 77 male and in 85 female patients.

The preponderance of male patients with typical ocular symptoms may be considered to depend on the greater disposition in general of the ocular apparatus of the male to dislocation of the lens. Likewise, a similar factor in the male may effect a pathologic shape of the auricle more easily than this is produced in the female. This theory does not necessarily mean that the chromosome which is affected in arachnodactyly has something to do primarily with the determination of sex, although the possibility of the location within the sex-determining

chromosome of those factors which determine the pathologic changes of arachnodactyly is not absolutely excluded by these findings. One would expect, however, a still more striking relation between the whole syndrome of arachnodactyly and sex. It is more probable, therefore, that the slight connection of some of the symptoms of arachnodactyly with sex may be better explained by a sex-linked predisposition to pathologic reaction of certain organs or parts of organs independent of the primary cause of the disturbance.

SUMMARY

The following groups of theories concerning the etiology and the pathogenesis of arachnodactyly are to be considered at the present time.

1. *Toxic or Infectious Damage.*—Toxic (e. g., alcoholic) or infectious (e. g., syphilitic) damage to the germ plasm before birth has been discussed in the French literature. According to prevalent opinion this is not probable, and it has been discarded as a theory in the most recent literature.

2. *Muscular Dystrophy.*—A relation of arachnodactyly to special forms of muscular dystrophy has received special consideration in papers published in England, but its existence is not probable, especially with regard to the complex of symptoms in various organs not related to the syndromes found in muscular dystrophies. In this connection, the fact deserves mention that the muscular deficiency in arachnodactyly is not progressive, in contrast to that seen in progressive muscular atrophy.

3. *Atavism.*—The theory of the reappearance of atavistic features (Poynton) has been replaced by the more modern theories of genetic mechanisms, especially in connection with the so-called degenerative states.

4. *Primary Hormonal Disturbance.*—This has been especially emphasized recently by Schilling and Fleischer. Schilling's second case should be mentioned as an example of hormonal disturbance in connection with arachnodactyly; there was dislocation of the lenses in a fast-growing 14 year old boy whose height at the age of 13 was 172 cm. The development of fatty tissue was poor, the formation of hair on the chest and in the axillas scanty and the distribution of hair feminine. Scoliosis and winged scapulas were present. The face was long and thin with a narrow jaw, the palate was highly arched and the chest was flat. There were a systolic murmur of the aorta and a low systolic murmur of the mitral valve. There were no clinical signs of a pituitary tumor. The borders of the sella were not sharp, no marked structure of the bones forming the contours. There was hyporeflexia, and the walk was similar to that of Friedreich's types. The spinal fluid contained increased protein; the urine contained chiefly gonadotropin (50,000 mice units). The "pregnancy reaction" of the urine was positive. Interferometric

reactions showed decomposition increased for ovary, adrenal and hypophysis and diminished for parathyroid. There were hypertension and progressive complaints and ataxia like that in locomotor ataxia. Ultimately the complete picture of Friedreich's ataxia was presented. There were no signs of acromegaly, dystrophia adiposogenitalis, diabetes insipidus or interrenalism.

The ocular symptoms consisted of bilateral dislocation, narrowness of pupil, large temporal conus and pigment deposits in the macula. The circumference of the head was 58 cm., of the chest 82 and 87 cm., of the calf 31 cm., of the middle finger, 12 cm. and of the large toe 7 cm. There was dryness of the skin, with pronounced striae distensae, the latter representing an important symptom of the hyperfunction of the anterior lobe of the pituitary gland.

In 1 of Fleischer's cases, similarly, bluish red lines in the shoulder region were noticed, resembling, in his opinion, the striae distensae in Cushing's disease (basophilic adenoma of the anterior lobe of the pituitary gland). The striae distensae of the skin, according to Fleischer, suggest a disturbance of the pituitary gland, and in connection with other endocrine disturbances are the etiologic factors of arachnodactyly. The secretion of gonadotropin in his case was slight in contrast to that in Schilling's; the sella was unusually broad and deep. In some of his cases the Abderhalden reaction showed irregularities of the hypophysis and the gonads. Fleischer leaned to the explanation given by Schilling, who stated the belief that hereditary hyperfunction of the eosinophilic cells or increased production of the growth hormone is a causative factor and that, accordingly, Marfan's syndrome represents in some cases disturbances of the hypophysis effected by nongenetic factors.

According to other investigations, arachnodactyly as primarily a hormonal disturbance is not entirely satisfying as an explanation for all features of the complete syndrome. Some authors, for instance Viallefont and Temple, basing their opinion on evidence of doubtful clinical value, such as the various sizes and shapes of the sella turcica, have been too ready to recognize in arachnodactyly a symptom of endocrine disturbance. This explanation, therefore, does not deserve serious consideration in view of the facts that arachnodactyly presents itself at the time of birth as a congenital, if not hereditary, malformation and that the changes in the size and the structure of the lens, zonular fibers and iris must be manifest many months before birth. The probability, however, cannot be excluded that, within the very complex pathogenic mechanism, endocrine functions are involved. The grouping of the syndrome among the actual diseases of the pituitary gland (anterior lobe), so that it is comparable, for example, to acromegaly or to Cushing's syndrome, is certainly not justified on such meager evidence.

Contrary to the explanation of arachnodactyly as a correlation disturbance in the inner secretory system in fetal life stands the fact,

mentioned by Fischbach, that arachnodactyly is usually fully developed and recognized at birth. According to Brandt the pituitary gland is developed in the eleventh week and achieves its relative maximal weight in the second month. The possibility that overaction of the gland would result in abnormal growth is contradicted by the fact that there is no acromegaly. Furthermore, in the cases of Salle, Boerger, Irvine-Jones and Rambar and Denenholz, the autopsies showed nothing abnormal about the endocrine glands, although it should be borne in mind that normal structure does not always exclude the possibility of functional correlation disturbances. In contradiction to the possibility of inner secretory disturbances, one must note that such disturbances in the fetus are compensated through the endocrine glands of the mother and that, therefore, hormonal dysfunction would show itself only some time after birth. Arachnodactyly cannot be viewed only as an anomaly of growth but must be considered as the accumulation of different congenital malformations, which are known to be lacking in inner secretory disturbances of the fetus.

5. *Disturbance of Nervous System.*—Arachnodactyly has been considered a primary disturbance of the nervous system. This theory was based on rather rare cases in which there were more or less typical symptoms referable to the nervous apparatus and resembling somewhat those of Friedreich's ataxia. It is not a feasible explanation for the majority of cases.

6. *Congenital Mesodermal Dystrophy.*—Weve's theory is of a prevailing congenital mesodermal dystrophy. On the basis of selective dystrophy of the mesodermal tissue, Weve explained the simultaneous involvement of bones, tendons, ligaments, muscles, connective tissues, fat, heart and blood vessels. Embryologically, however, this theory is unsound, for mesodermal involvement does not explain satisfactorily the pathologic changes of tissues ectodermal or entodermal in origin.

Kurz, for instance, stressed the ectodermal origin of the lens and the zonula. Mesodermal stripes as prohibiting factors in the development of the lens, advanced by Hess, von Hippel and Zeeman, cannot be ascertained by clinical inspection alone. The disproportion between the capsule of the eye and the lens, according to Thaden, Igersheimer and Fleischer, was contradicted by Kurz's first case, in which the intracapsularly extracted lens was rhomboid, with a coloboma-shaped depression in its temporal-lower part, but weighed 170.5 mg., which is within normal limits. The lens extracted from the second eye of the same patient weighed 168.7 mg., somewhat less than the first but still within normal limits. Marked changes in the zonula in the form of white and pigmented deposits, distinct stretching, rarefaction and tearing off of the fibers constituted hypoplasia as a primary disease, described by Vogt. In the discussion, Grosser pointed out that a congenital meso-

dermal dystrophy should result not only in skeletal and vascular but in urogenital anomalies. All the reports have uniformly failed to mention such complications. The findings in Kurz's case (lenses of normal size) were contradicted by Bakker, whose figures for four arachnodactylic lenses were decidedly below those for the normal (102, 112, 120 and 97.8 mg.) and for the lens in Lloyd's case (second series, case 3), which weighed 157 mg. The last of Bakker's lenses was cataractous and therefore subject to changes of a secondary nature; but the first three lenses exhibited were of equal weight and similar characteristics. There were slight curvature of the anterior and greater curvature of the posterior surface of the lens, and therefore the disturbances of the mesodermal posterior vascular net and the hyaloid artery led to the anomaly of the lens, a tissue of ectodermal origin. Bakker's findings seem to strengthen Weve's hypothesis.

Pino, Cooper and Van Wien took a similar stand in explaining the anomalies of the lens, the iris and the zonular fibers, basing them all on mesodermal maldevelopment. Congenital dislocation of the lens was explained as an anomaly of the embryonic vascular system causing developmental anomalies or weakness of the zonular fibers arising in the second or third month of fetal life; or the congenital mesodermal dystrophy might lead to dystrophic changes in the tunica vasculosa lentis and through these to changes in the lens and the iris. In both instances the disturbances of the mesodermal tissues might bring about anomalies of tissues of ectodermal origin, producing defects in the first instance, in the suspensory apparatus of the lens and in the second instance in the lens and the iris themselves. This explanation verges on Weve's conception, that the dislocation of the lens in cases of arachnodactyly is due not to a defect in the zonular fibers but rather to the smaller size and spherical shape of the lens.

Weve's explanation, however, is not considered satisfactory, not only because some of the typical symptoms probably are produced primarily by disturbances of the ectodermal germ layer but, and with still more reason, because the results of modern genetic studies prove that gene-conditioned anomalies are mainly not restricted to products of one germ layer. In other words, the symptoms represented by a single gene are not grouped according to the differentiation of the embryonic cells in different germ layers. The genic nature of the syndrome of arachnodactyly is rather certain, especially because of the numerous reports of cases in which this condition has been hereditary. A further objection to Weve's theory, raised by Fischbach, is that abnormal growth of the hands and feet cannot be blamed on the underdevelopment of the connective tissues.

7. Connection with Status Dysraphicus.—The status dysraphicus was linked with arachnodactyly by Passow, who pointed out the skeletal

characteristics as common to both conditions. The faulty closure of the neural tube (spinal dysraphia) was first recognized by Henneberg as an etiologic factor in hereditary neurologic diseases.

Syringomyelia consists in the proliferation of glial cells in the central region about the central canal of the spinal cord and the medulla. The gliosis breaks down and forms cystic cavities. According to Henneberg, the gliosis arises from embryonic cell rests within the spinal cord. The presence of cell rests depends on the faulty closure of the neural tube; hence the name dysraphia.

After the acceptance of dysraphia of the spinal cord as the underlying pathologic change of syringomyelia, Bremer scrupulously searched patients with syringomyelia and their families for developmental anomalies. His search revealed a span of the extended arms greater than the height, funnel chest with acrocyanosis, moist and cold hands, winged scapulas, webbed fingers and kyphoscoliosis, which might be the expression of trophic or muscular disturbances. A typical and frequent characteristic was a difference in the size of the breasts, the smaller breast exhibiting lighter pigmentation. Spina bifida, anomalies of the external ear and arched palate were other signs frequently encountered, usually referred to as degenerative stigmas. Family research showed that when typical syringomyelia occurred, other members of the family exhibited some of the symptoms, which were not progressive and, apparently, definitely hereditary. The structures involved—the sternum, breast, spine, spinal muscles, spinal cord and palate—all being midline structures, Bremer labeled the condition "status dysraphicus," expressing the belief that the syndrome is due to faulty formation of the spinal raphe.

The ocular signs occurring in arachnodactyly (ectopia of the lens, miosis and poor dilation of the pupil by atropine) are wanting in syringomyelia. Nevertheless, the syndrome is explained by Passow on the same basis, namely status dysraphicus, the dysraphia of the spinal cord producing a paralysis of the motor and trophic vasomotor fibers of the cervical portion of the sympathetic trunk. The disturbance in the tunica vasculosa lentis during embryonic life through the trophic vasomotor fibers results in microphakia and ectopia of the lens. Status dysraphicus, according to Passow, leads to Horner's syndrome and to heterochromia iridis, too, the former produced by paralysis of the motor fibers of the cervical portion of the sympathetic trunk and the latter by paralysis of the trophic vasomotor fibers of the sympathetic system. Passow examined patients and their families in cases of Horner's syndrome and heterochromia for signs of status dysraphicus and reported that he found them in a high percentage; singularly this seems to be contradictory to the fact that they rarely occur in persons with typical syringomyelia. Even in Bremer's studies of status dysraphicus they were found in but a small percentage of cases. Passow described hetero-

chromia iridis in 2 cases of arachnodactyly with dislocation (an observation also reported by Ennema and Charamis) and in later cases found the irises diascleral transilluminable, a symptom of dystrophy of the iris, and possibly of the ciliary body or the entire uvea, due to developmental disturbances, which is contrary to the theory of Weve, in whose opinion atrophy of the pigment layer of the iris is occasionally encountered. The dystrophy of the iris, a mesodermal growth disturbance, is therefore responsible for the dislocation of the spherical lens. In order to strengthen his views, Passow attempted to supply experimental proof. He excised, unilaterally, a part of the cervical portion of the sympathetic trunk in young animals, producing a lighter color of the iris on the homolateral side. In older animals no heterochromia could be produced. Therefore the paralysis of the cervical portion of the sympathetic trunk produces heterochromia only when it occurs before the development of the anterior layer of the iris and its pigment. Experimental heterochromia showed a decrease in the intensity of the anterior pigmented border layer, in the number of chromatophores and in the intensity of the posterior border layer.

If one assumes that arachnodactyly represents a microform of syringomyelia, or status dysraphicus, the logical sequence would be to demonstrate cases of arachnodactyly in which there is evidence of status dysraphicus, and vice versa, but the literature gives only scanty evidence of such cases. Passow called attention to Curtius' statement that multiple dysplasias or degenerative stigmas give rise to the suspicion that there may be a hereditary disturbance in development of the spinal cord, or incomplete closure of the medullary groove of varying degree. The symptoms in the two complexes are often similar, such as curving of the little finger, the muscles of which have their center near the ciliospinal center at the transition from the cervical to the thoracic segments of the medulla. Passow assumed the dependency, in the development of iris and lens, on nervous impulses from this region and hoped that autopsies in the future might furnish the necessary anatomic basis.

Passow's theory of a close connection between Marfan's syndrome and the microform of syringomyelia, or the status dysraphicus, is apparently based on the common presence of some features, which are also present in numerous and unrelated degenerative conditions. This is true especially of some of the so-called degenerative anomalies of the skeleton. The emphasis placed on single features appears exaggerated, and the conclusions as to the nature of such symptoms are far fetched. There are, on the other hand, so many features in the two syndromes which are directly opposed to one another that to construe a closer relation between the two appears unconvincing. One might mention only that many symptoms of typical status dysraphicus are unilateral, while the symp-

toms in arachnodactyly are bilateral. The type of bodily structure is absolutely different in the two syndromes; furthermore, there is not even a probability of proof that the symptoms of a bodily type, such as the extreme asthenic type, the basis for the aspect in arachnodactyly, could be effected by local vasoneurotic influences based on the nutritional status of the tissues, as assumed in Passow's theory.

8. *Degenerative Anomaly.*—Some authors place arachnodactyly among the degenerative anomalies, making it comparable with other conditions of atrophy or "abiotrophy" (Gowers), which may also be considered as special forms of a "status degenerativus" (Bauer). This point of view approximates closely the next group of theories.

9. *Constitutional Aberration of Anlage.*—In some of the earlier papers in the German literature one finds arachnodactyly placed among constitutional aberrations of the anlage (Thomas, 1914; Neresheimer, 1916; Thomas, 1926, and, later, especially Brock, 1927). This grouping, combined with the frequent report of the hereditary nature of the condition, especially in the American literature, gave rise to the most generally accepted and for the present probably the most plausible theory, i. e. that Marfan's syndrome is a form of multiple aberration of the anlage comparable to such syndromes as mongolian idiocy, the Laurence-Biedl-Moon syndrome and hypertelorism. This statement is not to be misconstrued as meaning that these syndromes are related to one another; they are different and independent syndromes which have only one thing in common, that they are or may be effected by a pathologic deviation in the character of the anlage. Their variegated character is explained by the localization of the damage in different chromosomes or in different parts of a single chromosome. Features common to several such degenerative conditions may be explained either by the assumption that two dissimilar pathologic conditions may involve an overlapping area or by the assumption that one organic symptom can be effected by different genetic causes.

As an explanation of this theory one may take the example of disturbances in growth which can theoretically be caused by (1) primary disturbances of the cell material in the growing tissues, especially of the skeleton (one then approaches the theories which place arachnodactyly somewhere in the vicinity of the chondrodysplasias, for instance the theory which Méry and Babonneix assumed when they coined the name hyperchondroplasia for the condition); (2) a disturbance originating in a genic upset through the hormonal system; (3) various possibilities according to the part which the abnormal function of the thyroid gland, the pituitary gland or some other member of the endocrine apparatus may play in development, or (4) a secondary involvement of the growing process by pathologic changes in the nutrition of the growing and differ-

entiating skeletal tissues produced by a disturbance of the vegetative nervous system and its relation to the circulatory conditions. In this way the genetic mechanism would form the basis for a pathogenic theory approaching that of Passow.

At any rate, the greatest credence is to be conceded those theories which consider a disturbance in the germ plasm as the basis of the syndrome. It is probable that such a disturbance is located primarily in the chromosomes, perhaps in one distinct chromosome whose representative functions govern all the symptoms which may be found in typical cases of arachnodactyly. The single chromosome carries many genes representing different characters in various organs and tissues. The idea of the free exchange of chromosomes is well known, but recently Morgan demonstrated that parts of the same chromosome may undergo shifting. However, in contrast to the free exchange of the entire chromosome, the shifting within a single one is not free, the chromosome chains changing their locations as units. The chains overlap, tear and lead to new combinations of chains (single or double crossing over). Hereditary factors located within the same chromosome are accordingly subject to coupling. The crossing over within the chromosome was applied for the first time in the ophthalmologic literature by Vogt as an explanation of arachnodactyly associated with dislocation of the lens. Mesodermal and ectodermal characteristics of the eyes and the extremities, the eyes and the heart and the eyes and the ears within the same chromosome would be linked accordingly. To mention a few of the possible combinations, I should like to call attention to the observations of Strebel and Steiger, who described ectopia of the lenses and the pupils dominant through four generations combined with rheumatic heart disease, and of von Roetth, who described a multiple cardiac condition (myodegeneration and mitral stenosis) with ectopia lentis simplex in members of a family with dislocated lenses. Polydactyly and syndactyly combined with ocular anomalies can well illustrate the possible linkages.

Depending on more or less extended damage within the chromosome, one or another symptom may be present or absent in a single case. It should be kept in mind, however, that the symptoms as they appear do not generally correspond to a single genic entity. For example, slenderness, tallness, a certain condition of the muscles, ligaments or joints, an unusual shape of the auricles, and deficiency in the suspensory apparatus of the lens may all be effected primarily by chromosomal factors. There may also be some interference by pathologic conditions in the endocrine, the nervous or the circulatory system, which in its turn may be influenced by genic factors, by abnormal aberrations in the structure of the chromosomal apparatus within the germ cells.

A pathologic condition in the germ cells may be inherited even if there is no evidence of a similar condition in the ancestry or within the

family. On the other hand, there is the possibility of a pathologic condition's starting in the germ cells by the process of mutation or idiovariation, which is independent of mixovariation produced by bastardization. The existence of mutation was proved by Morgan on Drosophila melanogaster and by Bauer on Antirrhinum. Mutation may result in the change of a single gene (factor mutation) or of the entire chromosome (chromosome mutation). The mutants usually are recessive, but a dominant characteristic is also possible (piebalding of Negroes). The mutations are even reversible in the experiment. A sort of intermediate theory could explain the mutations as arising from an unfavorable combination of genes in the germ cells from the father and the mother. The impetus to such pathologic mutations could be given in some cases by toxic or infectious influences on the germ cells, by which assumption one would come closer to the theories indicating a possible role played by alcohol or syphilis in the ascendants in cases of arachnodactyly, as occasionally mentioned in the French literature.

Ida Mann in a personal communication to Burch similarly placed emphasis on genic disturbances in congenital defects linked to a definite syndrome but took into account the possibility of a toxic or endocrine disturbance at a later date. This mechanism may involve mesodermal as well as ectodermal structures, the action being dependent on the period of development at which the action starts and on the structures undergoing rapid differentiation at the given time.

Whether or not there are cases of postnatal development of true arachnodactyly in a formerly normal person remains so far an unsolved problem, although in my opinion the probability of such an occurrence is extremely remote.

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CAROTID-CAVERNOUS ANEURYSM

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The literature on carotid-cavernous aneurysm has become so extensive that justification for the addition of another case to those recorded requires the presentation of unique features or elucidation on points that have not previously been clarified.

REPORT OF A CASE

J. L. S. S., a white man aged 52, was first examined on Sept. 23, 1939, exactly one month after he sustained a head injury from which he was unconscious for forty-eight hours. Roentgenograms showed a basal skull fracture. When he awakened, throbbing pain and a pulsating noise were present in the right side of the head. Diplopia was annoying, and his physician noted a difference in the size of the pupils, the right being larger than the left. He was kept in a hospital for two weeks. On September 15, a week after he returned to his home, the right eye began to protrude, and when this occurred the noise in the head disappeared but the throbbing pain became more severe. The vision became severely impaired when the swelling began.

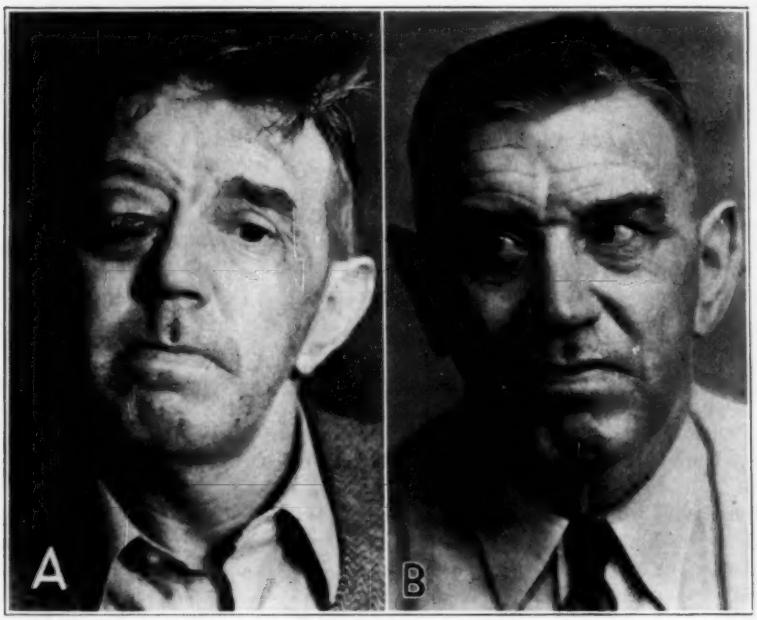
When the patient was examined on September 23 the vision was 12/400 in the right eye and 20/30 in the left without correction. There was obvious exophthalmos and decided swelling of the lids of the right eye. The lower tarsus and the lower fornix were everted owing to edema, and there was ptosis of the upper lid in addition to the edema (fig. *A*). No pulsation was detected even when pressure was exerted over the globe, and a bruit could not be heard with the stethoscope. The cornea was hazy, particularly in the lower portion. The pupil was fixed in mid-dilatation. Complete external ophthalmoplegia was evident. The ophthalmoscopic view was somewhat blurred because of the corneal involvement, but the retinal veins were obviously engorged; otherwise no abnormalities were noted. The tension measured 45 mm. of mercury (Shiøtz). There were no significant abnormalities of the left eye. Pressure over the right common carotid artery caused immediate cessation of the throbbing pain in the head.

Consultation was held by telephone with Dr. Frederick L. Reichert, of Stanford University School of Medicine, who happened to be in Honolulu. He advised frequent compression of the right common carotid artery for increasing lengths of time and felt that this procedure offered a chance of cure and would at least afford information as to the adequacy of the collateral circulation. If operation became necessary he advocated the use of fascia lata with incomplete ligation of the artery, future contraction of the fascia to accomplish complete closure.

One drop of 1 per cent physostigmine solution was used in the right eye three times daily for several days but had no effect on the tension or on the pupil. Compression of the right carotid artery was carried out three times daily for periods up to twenty-five minutes with no signs of cerebral anemia. By Sep-

tember 30 the pulsation had become less noticeable to the patient and some hope was felt that compression alone might cure the lesion. However, the throbbing pain soon regained its intensity in spite of compression up to forty minutes at a time several times daily. On October 7 ligation of the right common carotid artery was advised.

At operation, with the patient under local anesthesia this vessel was exposed and a strip of fascia lata passed around it and tied tightly with a single knot. The patient was watched for forty-five minutes and, as there were no untoward symptoms, a silk suture was placed through the knot in the fascia to fix it and the ends of the silk were left long so that they could protrude through the wound and allow rapid exposure of the ligature if necessary at any time.



A, preoperative photograph showing exophthalmos and edema; *B*, postoperative photograph, taken Sept. 6, 1940, showing residual paralysis of the external rectus muscle.

After operation the throbbing in the head diminished. There were no signs of cerebral anemia at any time. When the patient was discharged from the hospital on October 14 the protrusion of the eye had diminished about 50 per cent and some function had returned to all the extraocular muscles except the external rectus. The tension was 35 mm. (Shiøtz). The vision had improved to 20/200. The pupil was dilated and inactive, and examination with the slit lamp and the corneal microscope revealed adhesions of the pupillary border of the iris to the anterior part of the lens capsule extending from 2 to 11 o'clock. These were particularly dense from 2 to 7 o'clock, and this whole sector of the iris out to the limbus was atrophic and appeared to be plastered to the anterior surface of the lens. There were no deposits on the back of the cornea or cells in the aqueous. The tension had diminished to 28 mm. (Shiøtz) on October 23, and on

November 17 it was 27 mm. (Shiøtz) in each eye, a figure considered normal with the instrument in use. The adhesions from 7 to 11 o'clock broke up easily with the combined use of atropine and epinephrine bitartrate, but those about the atrophic portion of the iris remained fixed. An examination on October 30 showed the visual fields to be normal, but the campimeter chart showed a significant enlargement of the blindspot.

On December 1, for the first time on slit lamp examination, a fine anterior capsular opacity was found and under it a deeper faint subcapsular opacity, 1 mm. in width, extending from the center of the lens out to the pupillary margin at 8 o'clock. This opacity remained unchanged over several months of observation, and on March 2, 1940 the vision was 20/15 in the right eye with a correction of $+1.50$ D. sph. $\bigcirc +0.75$ D. cyl., axis 45 and 20/15 in the left eye with a correction of $+1.25$ D. sph. $\bigcirc +0.37$ D. cyl., axis 150.

The changes in the function of the extraocular muscles subsequent to the operation were of interest. From total ophthalmoplegia, function gradually returned, beginning with that of the internal rectus muscle. The inferior and the external rectus muscle were the last to recover (fig. *B*). Right hypertropia for distant and hyperphoria for near vision persisted until the middle of February 1940. The right eye was kept covered for several weeks after operation because of diplopia. Internal strabismus for distant vision was present from the time of discharge and has persisted until the time of writing. It naturally increased when the eyes were turned to the right. From Nov. 1, 1939 no patch was used over the right eye. The patient was able to get binocular single vision for near work after that time. However, he was not able to fuse distant objects and soon learned to suppress the image in the right eye. At present all hyperphoria has disappeared. There are 15 D. of right esotropia for distant vision and no phoria or tropia for near vision in the primary position. The patient gets diplopia only when the eyes are turned to the right. Orthoptic exercises were given for a time, but there was no improvement in the range of fusion or in the suppression; so they were discontinued. There is still some residual dilatation of the conjunctival veins.

COMMENT

No review of the literature on this subject is being undertaken here. While I was in the process of making such a study, the excellent survey of Sugar and Meyer [1] appeared, and it brought the matter up to date. For the first time in such a review emphasis was placed on increased intraocular tension. The mechanism of the production of such an increase is obvious; there is in many instances a marked increase in the pressure in the veins, with engorgement sufficient to interfere with the emptying of the anterior chamber. The literature abounds in cases in which the cardinal signs of acute glaucoma were displayed—dilated pupils, hazy corneas and obvious circumcorneal engorgement—but in most of the reports the intraocular tension was not mentioned. A measurement of this factor in every case reported would be of distinct value in the analysis of its frequency and importance. It is obvious that

1. Sugar, H. S., and Meyer, S. J.: Pulsating Exophthalmos, Arch. Ophth. **23**:1288-1321 (June) 1940.

there may be cases in which the increase is sufficient to make early therapy more imperative, and the tension might be a factor in determining the type of treatment to be instituted. In the present case, apparently no definite harm resulted from the persistence of a tension of 45 mm. (Shiøtz) for over three weeks.

The best therapy of carotid-cavernous aneurysm is by no means settled. This case is presented as an instance of an almost complete cure by ligation of the common carotid artery, the method that has the largest number of supporters. This method is felt to be relatively safe if the precautions used in the present case are observed, i. e. preliminary compression of the artery and careful observation of the patient for a considerable length of time after operation.

CONCLUSIONS

1. Measurement of the intraocular tension should be reported in every case of carotid-cavernous aneurysm.

2. Ligation of the common carotid artery with proper precautions is the method of choice as the first operative procedure in the treatment of this condition.

CYCLODIATHERMY

AN OPERATION FOR THE TREATMENT OF GLAUCOMA

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In this discussion it is our design: (1) to call attention to a recent development in the treatment of glaucoma; (2) to present a new, hitherto undescribed technic which, we believe, has many advantages over procedures used to date, and (3) to report our experiences with indications, complications and results based on operations in 32 cases. Furthermore, we should like to make some comments on the possible mode of action of the operation used and to report some experimental work.

The concept of the treatment of glaucoma by reducing the amount of aqueous formed is by no means a new one. In 1890 Wagenmann,[1] working with rabbits, observed that a reduction in intraocular pressure occurred when he cut the long posterior ciliary arteries. Recently Fortin [2] called attention to a similar observation. Heine [3] in 1905 first used the idea clinically when he performed cyclodialysis. He said, and there are many investigators who are still of the same opinion, that

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Dr. Albaugh is from the Department of Ophthalmology, Columbia University College of Physicians and Surgeons and the Institute of Ophthalmology, Presbyterian Hospital.

1. Wagenmann, A.: Experimentelle Untersuchungen über den Einfluss der Circulation in den Netzhaut- und Aderhautgefässen auf die Ernährung des Auges, insbesondere der Retina, und über die Folgen der Sehnervendurchschneidung, Arch. f. Ophth. (pt. 4) **36**:1-120, 1890.

2. Fortin, E. P.: Investigation sur le glaucoma, Buenos Aires, El Ateneo, 1939.

3. Heine, L.: Die Cyklodialyse, eine neue Glaukomoperation, Deutsche med. Wchnschr. **31**:824, 1905.

the reduction in pressure is due to an inhibition of the aqueous-producing activity of the ciliary body treated.

Shahan and Post [4] in 1921 observed that application of the thermophore near the limbus caused a relatively permanent reduction in pressure in normal rabbit eyes and in 2 human eyes with glaucoma.

In 1924 Verhoeff [5] reported a new method of attacking the ciliary body directly. He named this operation "cyclectomy," for it was literally an excision of a portion of the ciliary body. Although the operation has been too formidable for general use, the rationale for it is valuable. It is as follows:

1. The well known fact that injuries and inflammation of the ciliary body have a marked tendency to lower intraocular pressure.

2. Drainage into the subchoroidal space might be established by the operation.

3. Drainage might take place through the scleral wound if the uveal tissue was removed from its vicinity.

4. The vascular conditions in the ciliary body might be altered in such a way as to reduce the blood pressure therein.

5. Section of some of the ciliary nerves might reduce the intraocular pressure.

6. The operation might reduce the intraocular pressure in some unknown way, just as iridectomy lowers the pressure in glaucoma in some way not certainly known.

In 1925 Curran [6] reported an operation designed to accomplish three purposes: (1) to establish filtration, (2) to interfere with the function of parts of the ciliary body and (3) to produce a decompression staphyloma. The operation consisted in cauterization of an area over the ciliary body 8 to 10 mm. in diameter with the galvanocautery. However, it appeared that the essential condition for success was establishment of good filtration. Any effect from damage to the ciliary body seemed to be only temporary.

Hamburger,[7] in discussing a paper of Preziosi at the International Congress of Ophthalmology in Amsterdam in 1929, expressed the opinion that any inflammatory process in the ciliary body causes a temporary reduction of intraocular pressure. Verhoeff [5] had previously expressed the same opinion.

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4. Shahan, W. E., and Post, L.: Thermophore Studies in Glaucoma, Am. J. Ophth. **4**:109-118, 1921.

5. Verhoeff, F. H.: Cyclectomy: A New Operation for Glaucoma, Arch. Ophth. **53**:228-238, 1924.

6. Curran, E. J.: Subconjunctival Cauterization of the Sclera Over the Ciliary Body with the Galvano-Cautery to Reduce Intraocular Pressure in Advanced Glaucoma: Preliminary Report, Arch. Ophth. **54**:321-332, 1925.

7. Hamburger, in discussion on Preziosi, L.: Ergebnisse der Galvanokaustik bei der Glaucombehandlung, Zentralbl. f. d. ges. Ophth. **22**:779, 1930.

Fiore [8] at the International Congress of Ophthalmology in Amsterdam in 1929 reviewed the experiences he and his father had between 1909 and 1929 with a cauterization operation. This consisted in the application of a galvanocautery through sclera and ciliary body meridionally back from the limbus to the ora serrata. It was designed, he stated, to (1) make a destructive coloboma of the ciliary body to reduce edema and (2) cut the ciliary muscle ring and thus allow the circulation a freer flow. Fiore reported that he had done this operation on 177 eyes—most of them with acute glaucoma. It is likely that any success he achieved was due to the fact that there was an escape of vitreous. Furthermore, such an operation will probably not gain wide favor because the simple von Graefe iridectomy continues to give satisfactory results in acute glaucoma.

Recently in several papers Vogt [9] has discussed a new procedure which has created considerable interest. His operation consists in destruction of a portion of the ciliary body by means of multiple punctures (usually one hundred or more) with small diathermy needles of special construction. The area covered includes that between 3 mm. from the limbus and the ora serrata over one-third to one-half the circumference of the globe. This whole region is peppered with diathermy punctures. In 1939 Vogt's colleagues, Wagner and Richner,[10] reported that 47 operations had been done for various types of glaucoma. Of these, 72.3 per cent resulted in success. These authors also included a discussion of 2 cases which had been studied pathologically.

Because we had the work of Verhoeff in mind and because we had experienced the disastrous results of the usual therapy in cases of hemorrhagic glaucoma, early in 1938 we decided to apply the principles of the current operation for separation of the retina to the cyclectomy operation of Verhoeff. Later, Dr. David G. Cogan, having recently returned from a visit to Weve's clinic, suggested that we use a flat electrode in our work. He further assisted by making such an electrode for us.

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8. Fiore, T.: Igni-Skler-Ciliarotomie, Zentralbl. f. d. ges. Ophth. **22**:780, 1930.

9. Vogt, A.: Cyclodiathermy Puncture in Cases of Glaucoma, Brit. J. Ophth. **24**:288-297 (June) 1940; Die Zyklodiathermiepunkture (Z. D. P.) gegen Glaukom, Klin. Monatsbl. f. Augenh. **103**:591-599 (Dec.) 1939; Ergebnisse der Diathermiestichelung des Corpus ciliare (Zyklodiathermiestichelung) gegen Glaukom, ibid. **99**:9-15 (July) 1937.

10. Wagner, H., and Richner, H.: Zyklodiathermiestichelung, eine neue Glaukomoperation, Schweiz. med. Wchnschr. **69**:1048-1053 (Oct. 28) 1939. Richner, H.: Uebersicht über die modernen Glaukomoperationen mit besonderer Berücksichtigung der Zyklodiathermiestichelung, ibid. **70**:269-271 (March 30) 1940.

Gradually we developed and used two technics for cyclodiathermy. Simply for purposes of classification we have called them "perforating" and "nonperforating" cyclodiathermy. At first we used the descriptive term "diathermy of the ciliary body"; subsequently, after we had become cognizant of the work of Vogt, we adopted the anglicized form of the term which he had introduced: "cyclodiathermy."

NONPERFORATING CYCLODIATHERMY

The eye is anesthetized by instillation of 4 per cent cocaine and a retrobulbar injection of 1 cc. of 2 per cent procaine with epinephrine 1/1,000. It is especially advisable that epinephrine be included in the

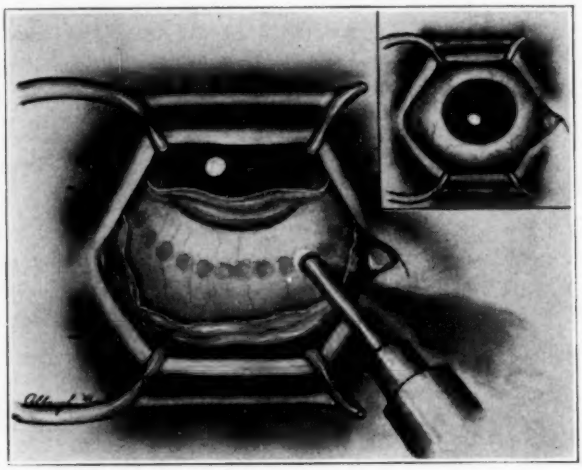

Fig. 1.—Drawing of nonperforating cyclodiathermy.

retrobulbar injection because it combats the tendency for tension to rise during and after operation. Because the eyes on which this operation is done are very sensitive, it is wise to wait a full ten minutes for good anesthesia.

The conjunctiva is incised 8 mm. from the limbus over a little more than one-half the circumference of the globe, and the sclera is bared to within 2 mm. from the limbus. It is a good policy to do the operation on the lower half of the eye, for later on it may be necessary to work on the upper half, as in cataract extraction. After the sclera is bared, the flat electrode (Weve type) is used over one half of the globe. It is necessary to apply it firmly against the sclera; otherwise there is no penetration of current and superficial searing is the only effect. Applications are placed at 4 to 5 mm. from the limbus immediately adjacent

to one another, one row being sufficient. Slight superficial searing of the sclera is a good criterion for the amount of current to be used. Because of the vast variation in diathermy apparatus, it would be dangerous to mention exact figures in terms of milliamperes. Furthermore, the amount of current passing through the electrode depends on the resistance and plate placement in the individual patient. On the Walker diathermy machine we have used the setting of 35 on the dial and applied current for eight to ten seconds for each application.

The conjunctiva is then closed with silk sutures. One per cent atropine is instilled, and a dressing is applied.

PERFORATING CYCLODIATHERMY

The preparation for this operation is the same as that for the nonperforating type. After the sclera is bared, a double row of Walker points is introduced at 3 and 5 mm., respectively, from the limbus at intervals of about 1 mm. Closure is the same as for the nonperforating operation.

POSTOPERATIVE COURSE

After experimentation with miotics, mydriatics and no medication at all, we have concluded that atropine is most satisfactory for use in the immediate postoperative period. There is damage to the ciliary body which is bound to result in a reactive cyclitis; hence the eye should be placed at complete rest. We have never observed any untoward signs which we could attribute to the use of atropine.

When perforating cyclodiathermy is done, we prefer to use a binocular dressing for twenty-four hours simply to keep the eye quiet. It has been our practice to keep the patient in bed for forty-eight hours in order to avoid a sudden rise in blood pressure which might burst intraocular vessels unsupported by normal or elevated pressure. We are more liberal with patients who have had the nonperforating operation. We use only a monocular dressing and allow the patient out of bed within twenty-four hours. This is especially advantageous in the treatment of older patients.

We have mentioned that when the nonperforating operation is done the intraocular pressure tends to rise. We believe that this can be explained as follows: coagulating current causes some puckering of the sclera; hence the total volume of the globe is reduced; thus the intraocular pressure is raised. Dr. John M. Wheeler, of New York, in some unpublished remarks observed and explained this phenomenon several years ago in connection with operation for separated retina. Particularly in cases of hemorrhagic glaucoma is it true that intraocular pressure is reduced only slowly after nonperforating cyclodiathermy.

Discomfort from the bullous keratitis which always accompanies this persistent elevation of pressure can be ameliorated by the use of hypertonic saline solution or saline ointment (Cogan[11]).

COMPLICATIONS

Cornea.—Reduction in corneal sensitivity over the area in which the operation is done is an almost invariable accompaniment of cyclodiathermy. (We cannot be certain that it occurs in 100 per cent of the cases because we did not observe it until several operations had been done.) Thus far it appears to be transitory. In only 1 case has it led to more serious consequences than bullous keratitis. Three weeks after operation patient 31 had a small ulcer of the catarrhal type near the limbus below, in the region of the operative site. However, it healed rapidly when local treatment was carried out.

As was mentioned, bullous keratitis is frequently present during the immediate postoperative period, and occasionally it may persist for several weeks if the intraocular pressure is at all elevated. We can offer one possible explanation for this phenomenon: As the nerves supplying the cornea are damaged, bullous keratitis may be a manifestation of trophic disturbances. This condition is a potential source of danger should an infectious process supervene.

In only 1 case we observed a transient parenchymal opacity near the site of operation, but this was present for only a few days.

Iris and Ciliary Body.—Hemorrhages may occur from the iris if the electrode is placed too close to the limbus. The explanation may be that the ciliary veins are occluded near their origin so that the resulting venous congestion is sufficient to rupture the iris vessels. Large intraocular hemorrhages may arise from iris or ciliary body as well as from any of the other intraocular structures when the perforating type of operation is used, owing undoubtedly to a sudden lowering of intraocular pressure with the result that delicate vessel walls rupture. Apparently a very mild iridocyclitis is present after operation, for those patients who were not given atropine postoperatively had some posterior synechias.

Lens.—Theoretically, one should expect that cataract might be caused by this procedure. Heat from the electrode might be sufficient to coagulate lens protein, or reduction in the amount or change in the quality of aqueous after operation might be a cause for a "cataracta complicata." We believe it would be unwise, however, to be dogmatic

11. Cogan, D. G.: Experimental Production of So-Called Bullous Keratitis, Arch. Ophth. **23**:918-925 (May) 1940.

on this point; for conditions which caused the glaucoma might also give rise to cataract. Therefore we have not attempted to evaluate our cases on this subject. We can say that none of our normal experimental animals on which the operation was done had a lens opacity. We are preparing to study further in experimental animals the amount of heat present in the lens during the operation.

Sclera.—Vogt said that he had 1 case in which scleral necrosis developed. We have not encountered this complication.

Sympathetic Ophthalmia.—It is generally considered that damage to the ciliary body increases the chance that sympathetic ophthalmia may develop. We have not seen this complication in our series of cases. Vogt has stated that the danger is minimal. In support of his belief he observed that thousands of similar operations have been done for separation of the retina with damage to uveal tissue. No case of sympathetic ophthalmia attributable to such an operation has ever been reported.

INDICATIONS FOR CYCLODIATHERMY

Hemorrhagic Glaucoma.—Cyclodiathermy is particularly indicated for this type of glaucoma. We prefer to use the nonperforating type. Other treatment has been completely ineffective. Magitot [12] has said: ". . . the only manner in which to relieve the patient is enucleation of the globe" (". . . la seule manière de soulager le patient est l'amputation du globe"). Duke-Elder [13] has expressed the same opinion. Bernard Samuels [14] and Duke-Elder [13] have indicated one reason why treatment has failed. It is that any operation which involves opening of the eye is likely to result in hemorrhage, and thus hemorrhagic glaucoma is superimposed on an already existent hemorrhagic glaucoma.

We have observed that in the majority of cases of hemorrhagic glaucoma the intraocular pressure falls only gradually over a period of days or weeks. In some few instances it may remain slightly elevated indefinitely but the patient is comfortable. Possibly this is due to destruction of nerves to the anterior segment of the eye. We now believe that in this type of glaucoma a cyclodiathermy of any less than one-half the globe is more often than not insufficient. Operation on

12. Magitot, A.: La tension pathologique, in Bailliart, P.; Coutela, C.; Redslob, E., and Velter, E.: Traité d'ophthalmologie, Paris, Masson & Cie, 1939, vol. 6, pp. 178-179.

13. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 3312.

14. Samuels, B.: Pathologic Changes in the Anterior Half of the Globe in Obstruction in the Central Vein in the Retina, Tr. Am. Ophth. Soc. **32**:369-388, 1934.

only one quadrant was inadequate in 7 of our cases. In 2 others trephining was done instead of further cyclodiathermy (listed as combined operation).

We cannot emphasize too strongly one precaution that must be taken before cyclodiathermy is done. *Intraocular tumor must be absolutely ruled out.* If there is any question as to a differential diagnosis, enucleation is the imperative procedure.

Glaucoma in Aphakia.—Cyclodiathermy is a valuable procedure to add to the surgical armamentarium for the treatment of glaucoma in aphakic eyes. Certainly filtration operations have a limited application. Cyclodialysis has been the operation of choice to date, but it is sometimes contraindicated. Furthermore, hemorrhage as a complication is the rule. Nonperforating cyclodiathermy avoids the complication of hemorrhage; therefore it is particularly to be recommended for diabetic patients or those having severe vascular sclerosis. Thus far, however, because we have wished to be conservative we have used cyclodiathermy only in cases in which cyclodialysis had failed or was definitely contraindicated for some reason or other. Perhaps a case in point will illustrate what we mean.

Case 31.—Mr. D. (from the service of Dr. John H. Dunnington, Institute of Ophthalmology), a 58 year old man, had glaucoma in the right eye. Medical treatment was ineffective. A corneal paracentesis was done. Vitreous escaped through the paracentesis wound, and a hyphemia appeared shortly. During the ensuing few days there were several fresh hemorrhages into the anterior chamber. The tension remained elevated. Because there was vitreous in the anterior chamber, any filtration operation was contraindicated. Because he had had recurrent hemorrhages in the absence of further trauma, we felt that cyclodialysis would be dangerous. Therefore a nonperforating cyclodiathermy was done on the lower half of the globe. Within forty-eight hours the tension was normal, and it has remained low ever since (two and one-half months). No further hemorrhages became manifest after operation.

Other Forms of Secondary Glaucoma.—Vogt has expressed the opinion that cyclodiathermy not only controls elevated tension but has a beneficial effect on iridocyclitis. We can agree with him to the extent that we have observed no deleterious effect in cases of glaucoma secondary to iridocyclitis and in a few have thought that there might be improvement attributable to the operation. One case is appropriate to mention:

Case 5.—Miss M. (from the service of Dr. Paul A. Chandler, Massachusetts Eye and Ear Infirmary), a 15 year old white girl, was injured in the right eye, and a traumatic cataract developed. Linear extraction was done. Later a persistent iridocyclitis and elevation of the intraocular pressure appeared. Intensive treatment, paracentesis and a filtration operation failed to control the elevated

pressure. Cyclodiathermy was done over three quadrants of the globe at intervals. During the six months since the last operation the tension has been normal. Although the field has suffered the vision has been 20/20 corrected. The iridocyclitis has subsided and is now quiescent.

Glaucoma secondary to roentgen ray therapy is another type very resistant to the usual forms of treatment. Cyclodiathermy may offer new hope for patients with this condition. One such patient in this series was successfully treated (a patient of Dr. Algernon B. Reese).

Primary Glaucoma.—Vogt has suggested that cyclodiathermy might compete with filtration operations in the treatment of this type of glaucoma because the danger of secondary infection or sympathetic ophthalmia is less after cyclodiathermy than after the other types of operation. We have preferred to remain conservative and have used cyclodiathermy only when other procedures have failed or were contra-

TABLE 1.—*Summary of Results*

Glaucoma	Perforating			Nonperforating			Combined			Totals		
	Success	Failure	Total	Success	Failure	Total	Success	Failure	Total	Success	Failure	Total
Hemorrhagic	5	1	6	3	2	5	1	0	1	9	3	12
Secondary	4	2	6	6	0	6	..	..	..	10	2	12
Primary	..	..	..	3	0	3	1	0	1	4	0	4
Buphthalmos	..	..	..	2	2	4	..	..	..	2	2	4
	9	3	12	14	4	18	2	0	2	25	7	32

indicated. However, in one circumstance we agree with Vogt. It is well known that filtration operations are not very successful in Negroes; the cicatrices rapidly become nonfunctioning. Cyclodiathermy may have a greater usefulness in this race.

Buphthalmos.—Two eyes were benefited and 2 were not. In retrospect, had one half of the latter 2 eyes been treated instead of only one fourth, success might have been achieved.

Our results are summarized in table 1. We considered a result as successful if the patient was comfortable under controlled tension. (Table 2 contains a detailed summary of the individual cases.) The result was a failure if the tension was not controlled, the patient was not comfortable or enucleation was done. The column heading "Combined Operation" refers to cases in which trephining was done when the tension was not sufficiently well controlled with cyclodiathermy. Operation was done on only one quarter of the globe in these cases. Had half the globe been treated, it is possible that subsequent operation would have been unnecessary.

TABLE 2.—*Summary of Cases* *

Case No.	Name and Age of Patient	Diagnosis and Therapy	Vision and Tension Before Cyclodiathermy	Cyclodiathermy	Result
1	McA. 69	Hemorrhagic, two weeks, miotic ineffective.....	20/100	1. ¼ upper temporal quadrant, perforating 2. ¼ lower temporal quadrant, nonperforating	12 days postoperatively, tension 11, vision 8/200; 3 mo. postoperatively, tension 28, vision 10/200; comfortable miotics
2	G. 81	Hemorrhagic, one week; miotics ineffective.....	Fingers at 1′; tension 55	¼ upper temporal quadrant, nonperforating	3 mo. postoperatively, tension 26; vision, fingers at 4′; no medication; mild iridocyclitis immediately after operation
3	P. 67	Acute attack in old chronic glaucoma; eight days; cataract; miotics ineffective	Good light projection; tension 48	1. ¼ upper temporal quadrant, nonperforating 2. Trephining six days later	10 mo. postoperatively, tension 19; no medication; cataract extraction to be done
4	N. 60±	Old chronic glaucoma; recent aphakia; vitreous hemorrhage six months later; cyclodialysis failed; miotics failed	Hand movements; tension 50	¼ lower temporal quadrant, nonperforating	3 mo. postoperatively, tension 36; hypermetropia; comfortable
5	M. 15	Secondary aphakia (traumatic cataract); cyclodialysis failed; other eye good	Hand movements; tension 40	1. ¼ lower temporal quadrant, nonperforating 2. ¼ upper temporal quadrant, perforating 3. ¼ upper nasal quadrant, perforating	Comfortable since third operation; miotics; 9 mo. postoperatively, tension 24, vision 20/20 corrected
6	T. 30	Hemorrhagic, diabetic; miotics ineffective; patient very uncomfortable	Nil; tension 48	⅓ nasal	9 mo. postoperatively, tension 48; vision, nil; comfortable
7	T. 30	Hemorrhagic, diabetic; trephining failed.....	20/70; tension 45	⅓ temporal	9 mo. postoperatively, tension 30, vision 10/200; hemorrhages still in fundus; miotic
8	D. 15	Secondary, old injury; miotics ineffective; no filtering operation for fear of sympathetic ophthalmia; other eye good	8/200; tension 46	1. ¼ upper temporal quadrant, nonperforating 2. ¼ lower nasal quadrant, perforating	1st held 10 mo.; vision 20/100, tension 15-30; sudden rise; 2d held 1 mo.; massive intraocular hemorrhage; enucleation
9	S. 70	Secondary aphakia; hemorrhagic, diabetic; hemorrhages in fundus	Fingers at 5′; tension 48	¼ lower temporal quadrant, nonperforating	2 mo. postoperatively, tension 22; 3 mo. postoperatively, tension 16, vision fingers at 3′
10	T. 64	Hemorrhagic; paracenteses and miotics failed.....	Hand movements; tension 70	Upper ⅓, nonperforating	Enucleation 16 days postoperatively; painful; hemorrhages from paracenteses
11	C. 60±	Hemorrhagic; miotics failed.....	Hand movements temporally; tension 65	¼ upper nasal quadrant, perforating	2 mo. postoperatively, sudden rise in tension; hemorrhage; enucleation
12	N. 60 (Negro)	Secondary aphakia; two trephining operations before; many paracenteses failed; only eye affected	4/200; tension 65	1. Upper ½, perforating 2. Lower ½, non perforating	2 mo. postoperatively, tension 22, vision 20/200; 1 yr. postoperatively, tension 15, vision, fingers at 2′; comfortable
13	B. 51	Hemorrhagic in only eye; diabetic; miotics failed....	20/200; tension 56	1. ¼ upper temporal quadrant, perforating 2. ¼ lower temporal quadrant, perforating	8 mo. postoperatively, tension 10, vision, light perception; 2¼ yr. postoperatively, tension soft; comfortable; (information by letter, unable to come in)

14	F. 56	Glaucoma capsulare; cataract; two trephining operations and paracenteses failed	Light perception; tension 65	¼ lower temporal quadrant, perforating	2 mo. postoperatively, tension 10; 1 yr. postoperatively, tension 19; 20 mo. postoperatively, tension 19, vision, hand movements; cataract
15	O'C. 67	Secondary aphakia; paracenteses and miotics failed	No light perception; stony	¼ upper temporal quadrant, perforating	Enucleated 4 days postoperatively
16	R. 59	Hemorrhagic and glaucoma capsulare; miotics failed	10/200; tension 60	¼ upper temporal quadrant, perforating	1 mo. postoperatively, tension 8; 8 mo. postoperatively, sudden bilateral keratoconjunctivitis; eye painful; enucleation
17	R. 5 mo.	Buphthalmos; trephinings and use of Verhoeff cannula failed	? vision; hard	Upper ½, nonperforating	8 mo. postoperatively, tension down, counting of fingers
18	R. 5 mo.	Buphthalmos; trephinings failed.....	? vision; hard	Upper ½, nonperforating	8 mo. postoperatively, tension down, counting of fingers
19	S. 28 mo.	Buphthalmos; two iridotases failed.....	Hard	Upper ¼, nonperforating	No appreciable result
20	S. 28 mo.	Buphthalmos; two iridotases failed.....	Hard	Upper ¼, nonperforating .	No appreciable result
21	M. 44	Secondary aphakia; high myopia with choroiditis; miotics failed	20/100; tension 50	¼ lower temporal quadrant, nonperforating	6 wk. postoperatively, tension 30, vision 20/200; 4 mo. postoperatively, tension 30, vision 20/200; miotic added
22	R. 67	Hemorrhagic; miotics failed.....	Fingers at 1'; tension 52	¼ upper temporal quadrant, nonperforating	Paracenteses; postoperatively, intraocular hemorrhage; enucleation 13 days postoperatively
23	C. 42	Secondary aphakia; intraocular hemorrhage; miotics, paracenteses and roentgen therapy failed	Good light projection; tension 42	¼ upper temporal quadrant, perforating	10 mo. postoperatively, tension 8, vision good light projection
24	K. 54	Primary chronic; two trephinings, two iridotases and cyclodialysis failed	20/70; tension 48	Nasal ½, nonperforating	5 mo. postoperatively, eye soft, vision hand movements
25	V. 58	Primary chronic aphakia; five years of trephinings, cyclodialysis, postsclerotomies	5/200; tension 42	¼ lower temporal quadrant, nonperforating	1 yr., tension 36, vision hand movements; comfortable
26	E. 51	Secondary; irradiation for carcinoma of antrum; sorbital failed; refused enucleation	Nil; tension 65	Upper ½, nonperforating	Tension down 10 days after operation, counting of fingers; comfortable; died 5 mo. postoperatively
27	D. 80	Hemorrhagic; miotics failed.....	Good light projection; tension 56	¼ lower temporal quadrant, nonperforating	1 mo. postoperatively, tension up again; trephining; under control since (3 mo.)
28	J. 48	Hemorrhagic; hypertension; miotics failed; refused enucleation	Light perception faulty; tension 85	Lateral ½, nonperforating	Tension down after 1 mo.; 2 mo. postoperatively, tension 26; comfortable; no medication
29	E. 52 (Negro)	Chronic primary; two trephinings and miotics failed	20/100; tension 40	Lower ½, nonperforating	1 mo. postoperatively, tension 15; 2½ mo. postoperatively, tension 15; comfortable
30	K. 53	Hemorrhagic, in only eye; diabetes not well controlled	5/200?: tension 90	Lower ½, nonperforating	22 mo. postoperatively, tension down, vision fingers at 2'
31	D. 58	Secondary aphakia; miotics failed; vitreous lost on paracentesis; spontaneous hemorrhages into anterior chamber	6/200; tension 56	Lower ½, nonperforating	Small ulcer below 2 wk. postoperatively; cleared on local treatment; 1 mo. and 1½ mo. postoperatively, tension down, vision 20/200; 2 mo. postoperatively, tension 20
32	L. 28	Secondary aphakia; diabetic; only eye; retinal detachment; painful; medication failed	Light perception	Lower ½, nonperforating	1 mo. postoperatively, tension 45; 5 mo. postoperatively, tension 10; comfortable; vision light perception

* Cases 1 to 25 inclusive are from the Massachusetts Eye and Ear Infirmary, Boston, and cases 26 to 32 inclusive from the Institute of Ophthalmology, Presbyterian Hospital, New York. Cases 26, 27, 30 and 32 are published with the permission of Dr. Algernon B. Reese, Dr. Frank Carroll, Dr. John H. Dunnington and Dr. Charles A. Perera, respectively.

COMMENT

We believe that our operations are less traumatic than the operation which Vogt has presented. In our opinion it is not necessary to make such extensive punctures. Furthermore, we wish to emphasize the advantages of nonperforating cyclodiathermy, which are dependent on the fact that the eye is not opened.

1. The anterior chamber is not collapsed. Although anterior peripheral synechias tend to form as a result of any operative procedure, certainly they are less extensive if the anterior chamber does not become flat. Kronfeld [15] has pointed out evidence to substantiate this hypothesis.

2. Since the eye is not opened, there is no sudden removal of support from the delicate walls of the blood vessels. Hence, hemorrhage is much less likely to occur as a complication either of the operation or in the postoperative period.

3. There is less chance for the aqueous to take on a more plasmoid character. The presence of increased amounts of protein and other coagulable substances would be likely to increase the extent of the anterior synechias formed.

4. There are no tracts into the interior of the eye through which infectious organisms could enter. Thus exogenous infection and sympathetic disease are virtually impossible.

5. Most patients affected with glaucoma are in the later decades of life. Long confinement brings a train of general complications such as psychosis, pneumonia or thrombophlebitis. It is therefore a distinct advantage to be able to allow the patient to resume normal activity as soon as possible.

We do not know the mechanism by which cyclodiathermy controls intraocular pressure. Verhoeff pointed out some of the possibilities (previously mentioned). We have approached the problem from two angles, the study of pathologic material and experimental work.

PATHOLOGY

One of our cases provided a good subject for study.

Case 16.—Mr. R. (Massachusetts Eye and Ear Infirmary), a 59 year old man, had hemorrhagic glaucoma in the left eye treated by cyclodiathermy. The tension was controlled for eight months. At the end of that time severe bilateral keratoconjunctivitis developed. The left eye became painful and was removed.

Figures 2 and 3 show the main changes. There is almost complete destruction of the ciliary body operated on. What mass is present consists for the most part of replacement fibrous tissue. The epithelial

15. Kronfeld, P.: Tr. Am. Acad. Ophth., to be published.

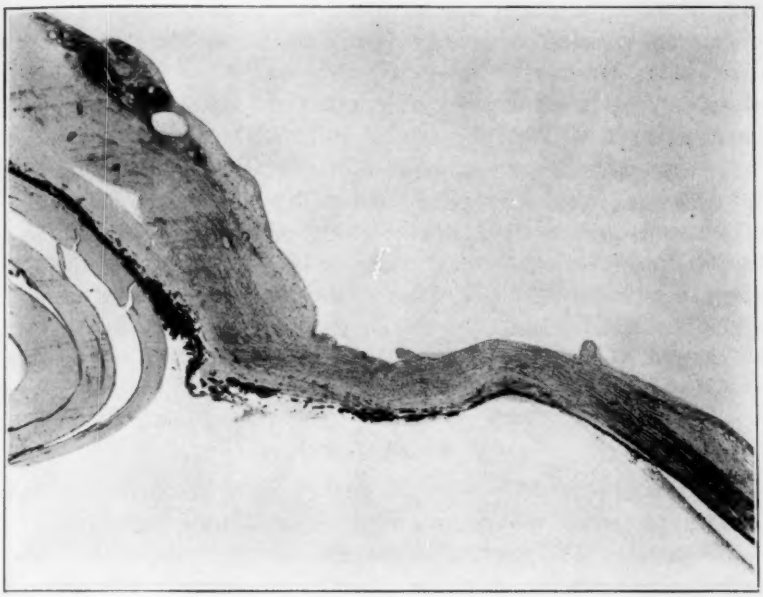

Fig. 2.—Section showing destruction of the ciliary body by cyclodiathermy. The section was from the Massachusetts Eye and Ear Infirmary, Boston, and was photographed at the Institute fo Ophthalmology, Presbyterian Hospital, New York.

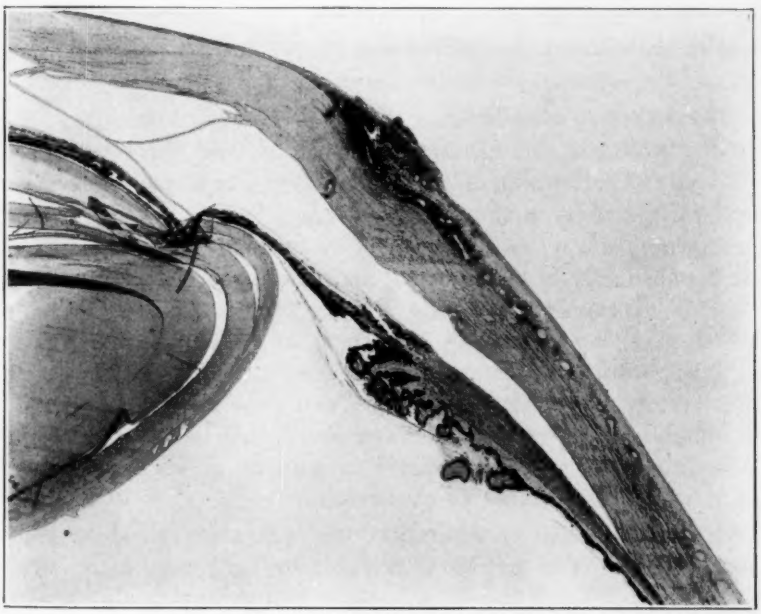

Fig. 3.—Section from an untreated area of the eye shown in figure 2.

layers of the ciliary body are disrupted and in places are lacking altogether. The destructive process is not limited to the corona ciliaris; in fact, it involves for the most part the pars plana. We are unable to determine from the sections what effect, if any, there was on the ciliary nerves.

We were able to study another eye which was removed a few days after cyclodiathermy. The earliest observable effects are on the pigment in the stroma and on the epithelial layers. The pigment in the stroma, which in the unaffected ciliary body is distributed in a netlike form, collects in spherical clumps. The epithelial layers are disrupted, and pigment is displaced into the anterior portion of the vitreous. As might be expected, there is some edema of the tissues, and small areas of necrosis can be seen in the stroma and in the muscle tissue.

EXPERIMENTS

In order to determine what the effects might be on normal healthy eyes, we performed nonperforating cyclodiathermy on a series of 6 normal rabbits. The animals were killed at intervals up to two and one-half months so that we might discover the sequence of reaction and healing. The microscopic changes, as well as the effects on intraocular pressure, check throughout with the observations on human beings. (The tension was taken with the Souter tonometer in all experimental animals because the curvature of the cornea in such animals is different from that in man and hence any readings with the Schitz instrument would be unreliable.) The rabbit does not seem to regenerate epithelium over the destroyed ciliary body as well as does man.

In our experimental animals we were particularly interested to see what the effects of the operation would be on the filtration angle and on the lens. There was no observable tendency to formation of anterior peripheral synechias, and the angle did not appear to be disturbed at all. Apparently any heat generated by current in cyclodiathermy is carried off rapidly enough so that the lens is not damaged. In none of our 6 experimental animals treated by cyclodiathermy did lens opacities develop. In treating 1 of them we deliberately increased the time of application of double the usual current to ten times the routine figure. When this animal was killed two months after operation the lens still showed no opacity. We are now trying to measure by means of a thermocouple the heat radiated to the lens by various amounts of current with various types of electrodes.

We have not as yet determined the effect of cyclodiathermy on accommodation. The pupillary reaction to light was more sluggish and the excursion was less on the side operated on than on the normal

side. However, the pupil in the eye operated on was round and contracted equally in all directions, the segment of the side operated on not lagging.

It might be possible that many of the structural changes in the ciliary body following cyclodiathermy could be trophic in origin owing to destruction of nerve supply. Cauterization sufficient to destroy the underlying portion of the retina was done on 3 normal rabbits both with diathermy and with actual cautery just at the equator under the horizontal rectus muscle on each side of the eye. These rabbits too were killed at intervals—the last two months after operation. In none were there microscopic changes in the ciliary body such as those observed after cyclodiathermy. Apparently, then, at least the visible changes are the direct result of heat and are not trophic.

CONCLUSIONS

1. The technic of cyclodiathermy is simple and does not require any extraordinary skill.

2. When nonperforating cyclodiathermy is used, complications incident to opening of the globe, such as hemorrhage, secondary infection and sympathetic ophthalmia, are practically eliminated.

3. Cyclodiathermy is the operation of choice for hemorrhagic glaucoma and should be used for other forms of glaucoma under the following conditions: (*a*) when other therapy, medical and surgical, has failed (particularly in Negro patients), and (*b*) when opening of the globe with consequent sudden reduction in the intraocular pressure is to be avoided.

4. Eyes sectioned some time after operation show that there is definite destruction of the ciliary body. Epithelial components do not regenerate completely; hence the membrane wall is broken down.

RHABDOMYOSARCOMA OF THE ORBIT

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It is well recognized by general pathologists that malignant tumors of definite myogenic origin may arise in different parts of the body—anywhere, indeed, that striated muscle exists. According to Jönsson, those arising in the skeletal musculature occur most commonly in the thigh, trunk and lower part of the leg, appear usually after the age of 40 and are invariably fatal.

The histologic features of these tumors, known variously by the terms rhabdomyoma, myoblastoma, malignant rhabdomyoblastoma, myoma malignum and rhabdomyosarcoma, have been described by many authors, including Montpellier, Roskin, Rakov, Cappell and Montgomery and others. Without going into the details of classification or into the theories of origin which have been propounded by various authors and on which there is yet no widespread agreement, it may be said that the striking histologic features of these tumors are pronounced polymorphism of the tumor cells, the presence of spindle cells tinctorially resembling muscle cells, the presence of giant cells and the existence in the cytoplasm of fibrils which are frequently but not always cross striated.

According to Haagensen, the tumors with less differentiation of the cells grow rapidly and cause death from generalized blood stream metastases within one year or less. The more differentiated ones grow relatively slowly and recur repeatedly over a period of years after local excision before metastases finally occur. They do not appear to metastasize to regional lymph nodes.

Haagensen also stated that there is a special type of rhabdomyosarcoma occurring in children in the testis, bladder, prostate, vagina and palate. This was recently further described and the cases added to by Cappell and Montgomery. It differs from the other types in that it usually shows cross striations and metastasizes not only through the blood stream but to regional lymph nodes.

From the Eye Institute of the Presbyterian Hospital.

Read at the Seventy-Seventh Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 30, 1941.

There are no reports of lasting cure of rhabdomyosarcoma. Irradiation was found to be virtually futile in the series reported by Rakov, Jönsson and others.

It is not surprising that rhabdomyosarcoma should occasionally be found in the orbit arising from the extraocular, or lid, muscles. In this paper we propose to review the literature on this subject, to report 5 additional cases studied by us and to summarize the clinical and histologic characteristics of this type of orbital tumor.

REVIEW OF REPORTED CASES

In the literature we have found reports of benign and malignant tumors of the lid and orbit originating from or composed in part or wholly of striated muscle under the titles rhabdomyoma, myoblastoma, rhabdomyoma malignum, myosarcoma rhabdomyosarcoma, etc. In the rather heterogeneous group of cases there appeared to be only 14 of clearly defined sarcoma arising from striated muscle which could properly be termed "rhabdomyosarcoma." All the other cases were regarded by us as instances of one of the following three types of tumor: 1. Benign tumors composed of adult striated muscle fibers arranged in an orderly, regular manner, properly termed rhabdomyoma (Jennings, 1895; Alt, 1896; Wible, 1918). 2. "Tumors" containing adult muscle tissue but with signs of inflammation such that their actual neoplastic nature might be doubted; these were considered probably to be pseudotumors (Bocchi, 1897; Posey, 1912; Pascheff, 1927; Mayer, 1929). 3. Tumors containing large amounts of fibrous or nerve tissue in addition to adult muscle tissue; these were considered probably to be mixed tumors or neurofibromas (Bietti, 1927; Schnaudigel, 1910 and 1913).

The 14 clearcut cases of rhabdomyosarcoma of the orbit were as follows:

1. Bayer in 1882 reported the case of a 3 year old boy who had had a swelling beneath the skin of the right lower lid for three months. There was no exophthalmos. At operation an infiltrating mass was found lying between the globe and the orbital floor, slightly adherent to the latter. Histologically the principal mass was composed of thin, newly formed muscular fibers striated transversely and in certain areas disposed very regularly. In addition to these spindle-shaped and ribbon-shaped cells, there were many round cells with pale round nuclei containing one or two nucleoli. The author mentioned also the frequent longitudinal fibrillation and great variation in the type of cell. There was no mention of recurrence of the tumor and no follow-up of the patient. Although the author did not speak of this tumor as sarcoma, we feel that future developments would have shown it to be such a tumor, since his descriptions and illustrations correspond to known examples of rhabdomyosarcoma.

2. The second report was by Zenker, who described in 1890 a recurrent tumor of the right orbit in a 7 year old boy who had had an exenteration of the orbit

one year previously. The tumor was first noticed when the patient was 5 years old. Two months after excision of the recurrent tumor there was another recurrence, and although the patient could not be followed further there were at that time severe frontal headaches and other symptoms indicative of metastases. Histologically the first recurrent tumor, which was the only one examined, was composed of numerous spindle cells with oval nuclei. Characteristic were the variation in the size of the cells and the cylindric forms. There were occasional long fibers. Longitudinal fibrillation and, less frequently, transverse striations were observed.

3. In 1903, under the title "Sarcome musculaire," López and Piquero reported the case of a 2 year old girl in whom a voluminous tumor of two months' duration was found in the upper portion of the left orbit displacing the globe downward. Only a portion of the tumor was removed, the eye being spared, and unfortunately there was no follow-up. The brief histologic description stated that the tumor was composed principally of striated muscle tissue and that among the large areas of connective tissue there were round and fusiform sarcomatous cells and a few spiral filaments of muscular tissue. The authors stated that the tumor was "fasciculated muscular sarcoma with round and fusiform cells."

4. In 1905 Mohr described, in a 4 year old child, a nut-sized tumor of three months' duration, palpable beneath the skin of the upper lid near the inner canthus. It was extirpated and recurred in three months. Histologically there were muscle fibers with fine cross striation in addition to two types of cells which stained similarly to muscle tissue with Van Gieson stain. Although the author stated that no definite sarcomatous tissue was found in the tumor, we believe from the description and clinical course that further study and follow-up would have proved it to be rhabdomyosarcoma. The interpretation of this case was made from brief abstracts, since the original article could not be obtained.

5. The first case in the English literature, and the only one in which autopsy was reported, was the case of Haythorn and Heckel in 1922. The patient was a 9 year old boy whose right eye had been prominent since receiving mild trauma on Sept. 12, 1912. When the patient was first seen, on October 2, examination showed exophthalmos of 3 mm. of the right eye, which was pushed downward and outward by a tumor palpable in the upper-inner portion of the orbit. On October 22 the orbit was exenterated. The tumor was nodular and found to involve the muscular attachment of the superior and the medial rectus muscle and probably part of the levator. There was definite attachment of the tumor to the upper lid. The superior oblique muscle appeared to lie on the surface of the tumor. On July 13, 1913 the orbit was curetted. On November 13 a recurrent tumor was present in the orbit, and the patient died on April 14, 1914 without further operation. Autopsy showed a tumor in the orbit with direct extension to the forehead, face, brain and pharynx and to the frontal, ethmoid, sphenoid and maxillary bones and metastasis to the left lung. The primary tumor as well as the first and the second recurrent tumor showed, even after lying for seven years in a specimen jar, embryonic cells with recognized cross striations. The lung metastasis contained "numerous cells which were shown to be striated muscle fibers, but here the striae were slightly more difficult to demonstrate."

6. Redslob in 1924 reported the case of a 5 year old girl in whom the parents had noticed a protrusion of the right eye for six weeks. Examination disclosed

exophthalmos due to a tumor in the outer-upper portion of the orbit. At operation, during which the tumor was excised, it was found to be adherent to the optic foramen and the sphenoidal fissure. A recurrence in six weeks necessitated evisceration of the orbit. The outcome was not stated. Histologically, the primary tumor contained pink-staining spindle-shaped and ribbon-shaped cells, many of which showed longitudinal fibrillation in the cytoplasm but none of which showed any cross striation. The character of the cell had changed completely in the recurrent tumor. No longer were there fusiform myogenous elements but only masses of round cells having the appearance of the cells of round cell sarcoma. Without the knowledge of the primary tumor, the author stated, he would have declared the recurrent tumor round cell sarcoma. It is entirely possible that the tumor reported by Redslob was leiomyosarcoma instead of rhabdomyosarcoma, as suggested by Mawas in the discussion of the article by Monbrun and Offret.

7. In 1929 Dérer reported a case of "rhabdomyosarcoma orbitae melanoticum." Although we have been unable to obtain the full case report, we have learned from abstracts that the patient was a 17 year old boy in whom the tumor nodule involved the inferior rectus muscle. Seven weeks after its extirpation a large recurrent tumor forced exenteration of the orbit. There had been no recurrence after two and a half years. Histologically, the author described a delicate connective tissue capsule beneath which there was a tumor having a typical small cell sarcomatous structure and cross striped muscle fibers. The tumor was deeply pigmented, the pigment being disseminated finely as well as lying in large clumps among the cells and muscle fibers. Lack of further information necessitates our acceptance of the author's diagnosis in this case.

8. In the Spanish literature 3 cases have been reported, all of them as instances of "rhabdomyoma" despite the clearcut sarcomatous nature of the tumors. The first was that of López Enriquez (1933), whose patient, a 10 year old boy, had had a swelling in the upper-inner portion of the left orbit for five months. The tumor grew until it was the size of a walnut. There was no change in size after exploratory puncture and roentgen therapy. When first seen by the author, two and a half months after onset of symptoms, the tumor descended from the superior conjunctival fornix to cover the lower lid and extended outward to a point halfway down the nose. The tumor was removed. The ultimate outcome was not stated. Histologically, the author described a moderate connective tissue capsule and marked polymorphism of the cells, which showed all transitions from the small undifferentiated myoblasts to the more differentiated cells containing myofibrils and cross striations. The nuclei had a sarcomatous appearance, and many cells had ten or more nuclei. The author advocated the Río-Hortega stain for demonstrating the typical myofibrils and transverse striations, which are shown in the illustrations.

9. The report by Mier (1934) was on the contents of an exenterated orbit taken from a museum jar, and no history was available. He was able to demonstrate three types of cells: (1) round or elongated cells without striation but with a chromatic reaction which showed their myogenic nature, (2) fusiform striated cells and (3) large round or pear-shaped cells with myofibrils. This author also advocated the Río-Hortega stain.

10. In 1935 Pupo reported the third case in the Spanish literature, under the title "Rhabdomyoma of the Lid." This case is interesting in that the patient was

a woman 70 years of age who had a walnut-sized tumor beneath the skin of the upper lid; it was first noticed one year previously and had grown rapidly in size. Without any evidence of metastasis the patient died of bronchopneumonia two months after biopsy. Histologically, there were two types of cells: There were (1) round cells, varied in size, with some of giant proportions; there was occasional vacuolation, and with the silver technic of Río-Hortega both long and cross striations were visible. There were (2) fusiform cells, varied in size, with and without striations, occasional elements being tripled in size. There were also areas of myxomatous degeneration and of necrosis.

11. Sjögren in 1935 made a complete and lengthy report on a case under the title "Myoblastoma malignum orbitae." His patient was a boy of 8 years with a tumor lying against the roof of the left orbit. The tumor recurred twice after excision and finally even after exenteration of the orbit, and the patient died of metastases seven months after exenteration and nineteen months after onset of the first symptoms. Histologically, the first and the second recurrent tumor showed a similar varied structure. Parts of the tumor contained large round or oval cells with one or more irregularly formed central or peripheral nuclei. Scattered among these cells were ribbon-shaped cells containing vacuoles, small nuclei and both longitudinal and transverse striation. In other parts of the tumor there appeared great polymorphism of the cells, with numerous polymorphonuclear giant cells and rich connective tissue participation. The final recurrent tumor had a homogeneous structure and the histologic appearance of sarcoma. The author stressed the fact that without knowledge of the previous biopsies the last recurrent tumor would have been diagnosed as typical round cell sarcoma.

12. Monbrun and Offret in 1937 described at length the case of a 9½ year old girl who had a swelling at the upper-inner portion of the right orbit which grew into the superior conjunctival fornix to project between the lids. In May 1936, four months after onset of the symptoms, radium needles were implanted in the tumor for nine days. The tumor subsided, leaving only an indurated focus at the inner angle of the orbit. In September, however, there was a rapid recurrence and an attempt was made at local excision. One month later there was a local recurrence, and systemic signs of metastases developed. The patient left the hospital; so the subsequent outcome was unknown. Histologically, the author described acidophilic muscle cells at all stages of development, with both longitudinal and transverse striation. There were also many multinucleated giant cells.

13. In the discussion of the paper of Monbrun and Offret, Mawas reported another case, that of a 5 year old boy in whom removal of the tumor was followed in a few weeks by recurrence and death. Histologically, Mawas described longitudinal and cross striation shown well by iron hematoxylin, areas in which the syncytium was rather loose and the cells contained large vacuoles and others in which the cells had monstrous lobulated nuclei.

14. In 1939 Castren and Teräskeli described the case of a 3 year old boy in whom the right upper lid had for one month been swollen and a reddish tumor noted underneath it. The parents felt that the patient's right upper lid had been thicker than the left from birth. Examination showed a mass in the upper fornix extending the whole breadth of the lid and back into the orbit. The portion projecting between the lids was excised, and after histologic examination a more thorough local excision was done. Ten months later another tumor appeared, and all tissues were removed to a depth of two thirds of the orbit. Swelling and exophthalmos, which appeared in ten days, were reduced by 6,100 roentgens of

irradiation, but after two months another recurrence necessitated exenteration by electrocoagulation. Another tumor, one week later, was not influenced by implantation of radium, and the patient died one year and eight months after the discovery of the tumor. Histologically, the primary tumor consisted largely of pink-staining spindle-shaped cells with longitudinal and cross striations. A small part contained polymorphous undifferentiated cells which did not have the staining characteristics of muscle tissue. There were occasional giant cells. Examination of one of the recurrent tumors showed a different picture. There were no highly differentiated cells of the muscle type, but instead the tumor, according to the author, resembled cellular infiltrative high grade anaplastic sarcoma. The tumor cells were immature, small, round or spindle shaped, contained numerous mitoses and did not show with the Van Gieson stain the characteristics of muscle tissue. The author stressed the fact that the primary tumor and the recurrent tumor were so different that one would not have suspected a muscle origin from examining only the second tissue.

FIVE ADDITIONAL CASES

Five additional cases of rhabdomyosarcoma of the orbit which we have studied are reported as follows:

CASE 1.—L. W. was an 8 year old boy whose parents had noticed a progressive swelling of his left upper lid for three months prior to the first examination, on July 1, 1938. Examination showed a firm, lobulated, nontender and nonfluctuant mass beneath the left upper lid beginning just above the internal canthal ligament and extending upward and slightly outward to pass behind the upper orbital margin. Only a portion of the tumor could be palpated. It was immobile and not attached to the skin. There were slight ptosis of the left upper lid, slight exotropia and right hyperphoria. On July 7 the tumor was excised, and it appeared to be attached to the superior oblique muscle.

On November 30 a recurrence in the form of a pea-sized subconjunctival tumor over the internal canthus was excised, and the orbit was treated with a total of 3,600 r of irradiation between Feb. 10 and 24, 1939.

On May 22 palpation of the orbit revealed a firm, nodular, freely movable mass beneath the left upper lid, protruding beyond the orbital margin and apparently largest temporally, where it lay just beneath the conjunctiva in the upper fornix (fig. 1). There were 4 mm. of exophthalmos, ptosis and no enlargement of preauricular or cervical lymph nodes. Roentgenograms of the orbit showed an increase in density of the soft tissue, a shallow fossa in the roof of the orbit and deformity of the lamina papyracea. There was no destruction of bone. On May 26 complete exenteration of the left orbit, including the cilia line of both lids, was performed and a Thiersch graft from the thigh applied to the orbit. There was no local or general evidence of recurrence May 10, 1941, two years after the operation.

Microscopic Examination.—Primary Tumor (fig. 2): The tumor was composed chiefly of large rounded or globular cells with sharply defined cell membranes and eccentrically placed nuclei, each furnished wtih a single large nucleolus. The cytoplasm was acidophilic. In many cells close examination disclosed many granules and filaments arranged either in whorls or in a parallel longitudinal manner and best seen in the phosphotungstic acid–hematoxylin stain. Scattered among these cells were spindle-shaped and ribbon-shaped cells of varying sizes, many of them showing longitudinal as well as transverse striation only with stains containing iron hematoxylin. There were also occasional giant cell multinucleated forms, some of

Fig. 1 (case 1).—Photograph taken May 23, 1939, just prior to exenteration of the orbit, showing the appearance of the subconjunctival extension of the second recurrent tumor in the outer-upper portion of the left orbit.

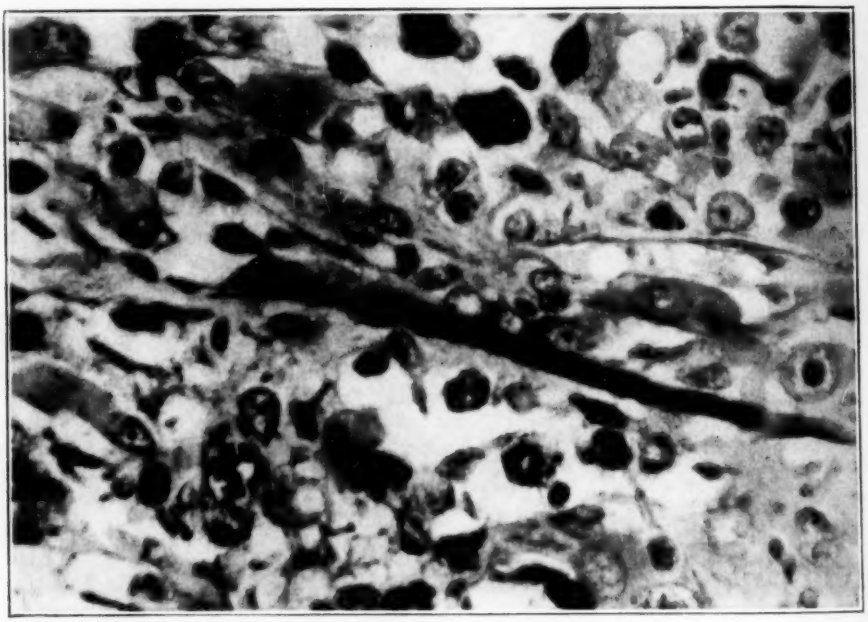

Fig. 2 (case 1).—Section of the primary tumor, showing several of the large cells with oval nuclei and abundant cytoplasm (Masson stain; × 540). In the center is an extreme example of a highly differentiated tumor cell, with cross striation of its cytoplasm, which has been retouched by the artist.

which had vacuolated cytoplasm. Mitoses were rare. In a few peripheral areas there were undifferentiated tumor cells with small round nuclei and without acidophilic cytoplasm or any of the distinguishing features of muscle cells. There was practically no connective tissue stroma. Although apparently circumscribed, the tumor occasionally showed invasion of its capsule and even penetration outside of it.

First Recurrence: The tumor was composed of loosely arranged small cells with small round nuclei and scanty, more basophilic cytoplasm. Only a few ribbon-shaped cells with acidophilic cytoplasm were seen.

Second Recurrence (fig. 3): The large tumor mass had now a more homogeneous appearance and was composed chiefly of closely packed round or cuboid cells with

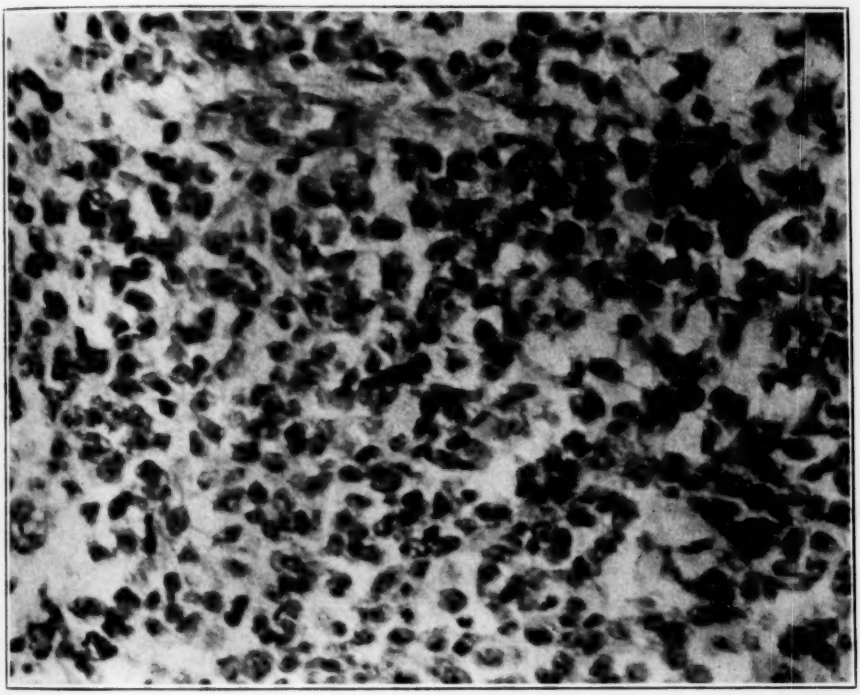

Fig. 3 (case 1).—Section of the tumor removed at exenteration of the orbit (hematoxylin and eosin stain; ×325).

small oval or round nuclei and basophilic cytoplasm. Numerous cells contained vacuolated cytoplasm (glycogen?). The tumor was traversed by numerous fibrous septums, and the cells in certain areas had a distinct alveolar arrangement. There were occasional large cells with several nuclei. Mitoses were rare. Only rarely were there found small pink-staining ribbon-shaped cells suggestive of muscle cells. The globe was normal.

Comment.—The changed character of the cell type in the recurrent tumors in this case is of particular interest. Without the knowledge of the microscopic appearance of the primary tumor the muscle derivation of the recurrent tumors would not have been suspected.

CASE 2.—B. P., a 4 year old boy, began to have ptosis of the right upper lid on or about Sept. 15, 1937. This was followed soon after by the appearance of a subcutaneous lump near the outer canthus, which grew in size. In October exophthalmos developed. Examination disclosed the right eye to be pushed forward, upward and nasally by a firm lobulated tumor. The globe was normal. Roentgenograms showed clouding of the right antrum but no destruction of bone in the orbit. On November 19 exploration through an incision in the lower fornix disclosed a thick, firm, fleshy tumor extending back into the orbit and involving the lid and conjunctiva so that only a portion could be removed (fig. 4). Between December 3 and December 28 the patient received fractionated doses of roentgen rays to the right orbit until a total of 3,600 r had been received.

Apparently there was complete clinical regression until March 1, 1939, at which time exophthalmos reappeared and a mass became palpable above and medial to

Fig. 4 (case 2).—Photograph taken Nov. 30, 1937, showing the right eye displaced forward, upward and nasally by the tumor in the outer portion of the orbit.

the globe, which appeared depressed. Between March 3 and March 17 the patient was given additional roentgen therapy, receiving a total of 2,750 r. No clinical regression was noted during treatment; so on March 20 exenteration of the orbit was performed and a Thiersch skin graft applied. The patient was last seen on March 13, 1941, at which time his general health was good and the orbit showed no evidence of a recurrence. This was two years after the operation and three and a half years after the tumor was first noticed.

Microscopic Examination (fig. 5).—Only the material removed at exenteration was obtained for examination. The tumor was composed of closely packed, interlacing bundles of large, elongated, spindle-shaped and ribbon-shaped cells which varied greatly in relative size. Most of them had large ovai or blunt-ended nuclei with from one to three nucleoli. Mitoses were rare. Occasional large cells with several nuclei were seen. The cytoplasm was distinctly acidophilic and with differ-

ential stains gave the characteristic reaction for muscle tissue. Occasionally the cytoplasm contained large and small vacuoles. Scattered throughout were smaller, intensely acidophilic ribbon cells. With the Masson stain fine longitudinal fibrillation of the cytoplasm was frequently seen, but only after diligent search could several cells be found with definite transverse striation. Differential stains showed also a great number of collagen fibers, which appeared to separate each cell. At its margins the tumor was sharply circumscribed, but it did not appear to be actually encapsulated. The globe itself was normal.

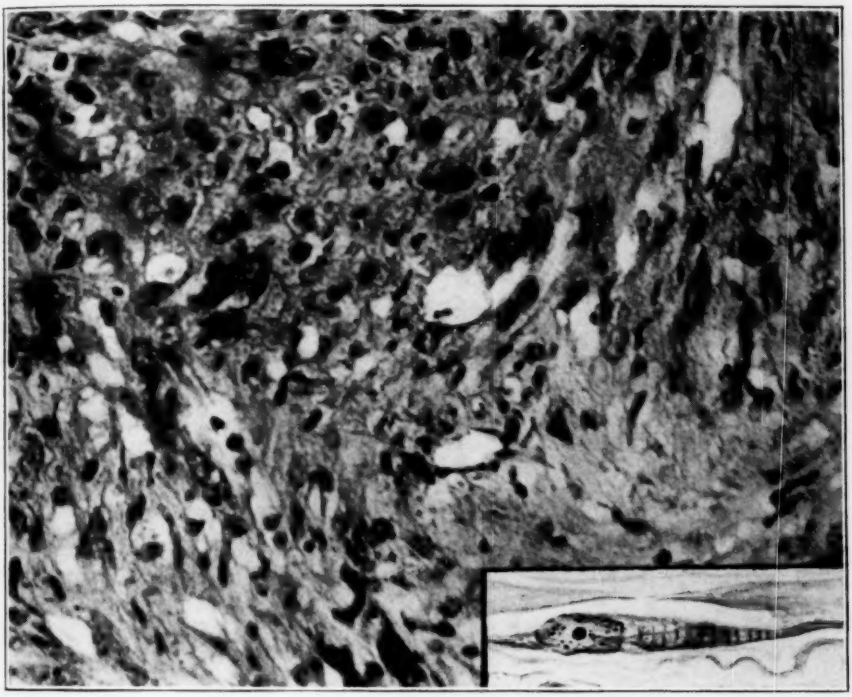

Fig. 5 (case 2).—Section of the tumor removed at exenteration of the orbit (hematoxylin and eosin stain; × 325). The inset is a drawing of a tumor cell containing typical cross striations (Masson stain, oil immersion).

Comment.—An unusual clinical feature of this case was that after irradiation there was complete clinical regression of the tumor for fifteen months.

Case 3.—F. A., was a 4 year old girl whose parents noticed a sudden bulging of her left eye three weeks before examination on July 26, 1938. There was marked proptosis of the left eye, which was pushed forward, downward and nasally by a tumor in the upper temporal aspect of the orbit. There was pronounced papilledema of the left eye. Roentgenograms of the skull showed no bone erosion of the orbital walls. On August 9 the lacrimal gland and several pieces of tumor

were removed through a conjunctival incision. Examination on August 17 showed a distinct increase in the exophthalmos of the left eye, prolapse of the conjunctiva, exposure keratitis, inability to close the lids, marked limitation of motion in all directions, papilledema and the presence of a diffuse, firm, palpable orbital mass, largest in the upper portion (fig. 6). On August 22 exenteration of the left orbit with application of a Thiersch graft from the thigh was performed. On October 6 a recurrent tumor was noticed in the apex of the orbit and directly beneath the skin of the upper lid. The patient was given a total of 3,000 r of irradiation centered directly over the left orbit. There was steady progression of the tumor under treatment; so on November 4 further excision was undertaken. At this time it was found that the growth appeared to be involving and destroying bone in the orbital walls and to be extending intracranially through the optic foramen. On November 8 radon seeds were inserted into the orbital tumor, but the course was rapidly downhill, the patient having cachexia, fever, purpura and general debility. She died on

Fig. 6 (case 3).—Photograph taken in August 1938, just prior to exenteration of the orbit, showing the proptosis and corneal ulceration produced by the rapidly growing tumor in the upper portion of the left orbit.

Jan. 30, 1939. Autopsy showed metastases to the pleura, lungs, liver, stomach, ovaries, ribs and skull and to the retroperitoneal and mediastinal lymph nodes.

Microscopic Examination.—Exenteration Material (fig. 7): The bulk of the tumor was composed of bundles of closely packed spindle-shaped cells cut in all directions. The densely staining nuclei were large and oval and contained one or more nucleoli and coarsely granular chromatin. The cytoplasm was scanty and granular and only moderately acidophilic but gave the characteristic reaction of muscle tissue with the Van Gieson stain. The cell borders were ill defined. There were many large multinucleated cells. Mitoses were uncommon. In certain scattered areas there were a few small ribbon-shaped cells with small dark nuclei and more decidedly acidophilic cytoplasm. With the special stains occasional longitudinal, but not transverse, striation was found. The tumor cells were

accompanied by a small number of collagen fibers. The globe was normal except for a large corneal ulceration.

First Recurrence After Exenteration (tumor excised on November 4): The entire nodule of the tumor was composed of myxomatous tissue in which there were many spindle-shaped and ribbon-shaped cells showing a more pronounced acidophilic cytoplasm than in the previous specimen. Special staining revealed frequent longitudinal fibrillation, and several cells and fibrils showed well developed transverse striation in addition.

Autopsy.—The infiltrative metastasis in the wall of the stomach was composed of compactly arranged bundles of spindle cells. The metastases in the liver, lungs,

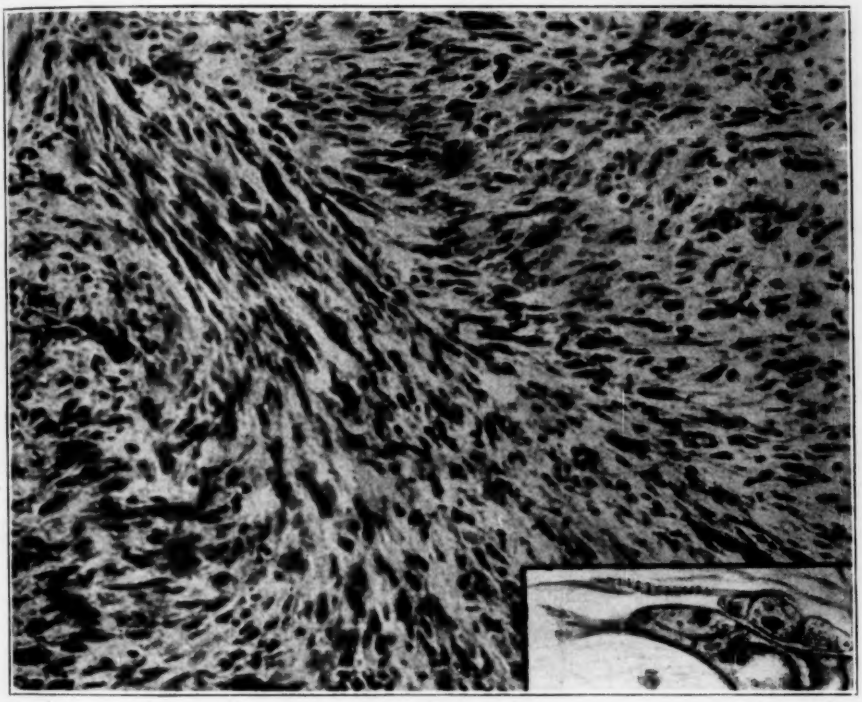

Fig. 7 (case 3).—Section of the primary tumor (hematoxylin and eosin stain; ×225). Cross striations were not found in the primary tumor but were present in the recurrent tumor. The inset is a drawing of a multinucleated cell in the recurrent tumor, showing well developed cross striations.

ovaries and lymph nodes all showed masses of small round cells with large, densely staining nuclei and scanty, frequently vacuolated cytoplasm with little resemblance to the orbital growth and none to muscle tissue. Lack of material prevented further study of the metastases by special stains.

Comment.—This was a rapidly growing and extensive tumor which was so far advanced at the time of exenteration that recurrence was to be expected. Although the histologic appearance of the primary tumor

was entirely consistent with the diagnosis of rhabdomyosarcoma, definite transverse striation of the cytoplasm was found only in the recurrent tumor. Another noteworthy feature was the round cell character of the metastases.

CASE 4.—This case is presented with permission of Dr. M. L. Kauffman, of Jenkintown, Pa. We have examined the slides in our laboratory.

The history furnished by Dr. Kauffman is as follows: "The patient, a 6 year old boy, was first seen on Nov. 18, 1940; the left eye had been sore and prominent

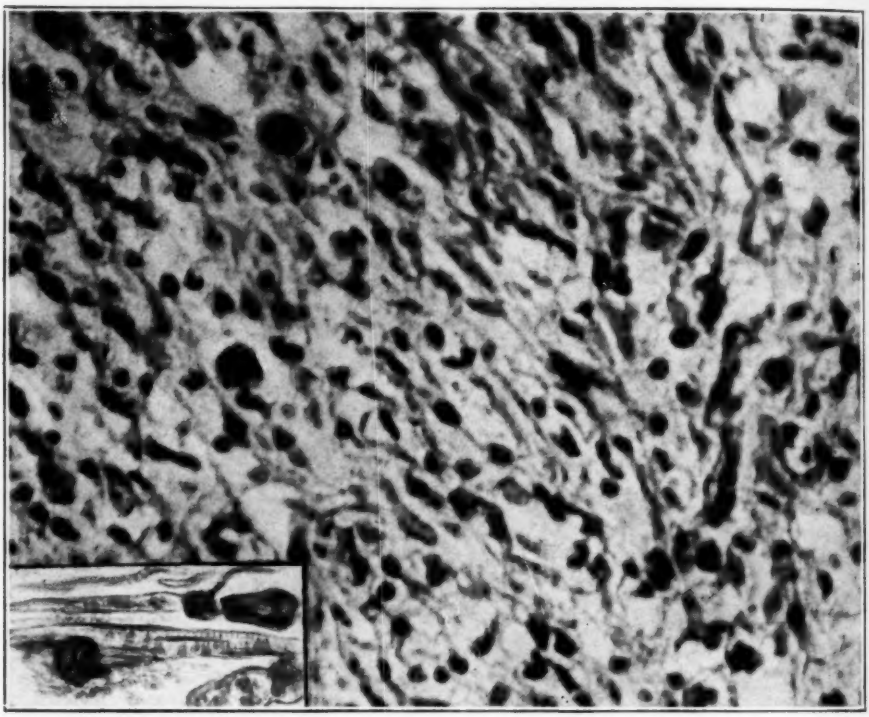

Fig. 8 (case 4).—Section of the primary tumor (hematoxylin and eosin stain; × 400). The inset is a drawing of one of the ribbon-shaped cells to show the cross striations.

for five weeks. Examination showed vision to be 20/20 in the right eye and 20/50 in the left. The globe was pushed upward and proptosed 5 mm. by a mass easily palpated in the lower-inner portion of the orbit. The patient had no diplopia, but the left eye was slightly up with the cover test. The left fundus showed venous engorgement and slight edema of the nerve head. On December 11 the tumor was removed through a cutaneous incision in the lower lid and was found to be pear shaped, measuring roughly 2.5 by 5 cm., with the base forward

and lying in the inner-lower portion of the orbit. After histologic examination exenteration was advised but was refused by the patient's parents.

"The vision returned to 20/20 and the edema of the fundus disappeared. In the course of two months 6,000 r was directed from several directions to the portion of the orbit from which the tumor was removed. At the end of this time the vision was reduced to 20/30 in the left eye. A definite recurrent mass was palpable beneath the wound on March 22, 1941, and on March 26 the orbit, including the lower lid, was exenterated. The upper lid was spared. The tumor mass this time measured roughly 4.5 by 2.5 by 1.5 cm. The pathologists felt that the excision was wide of the tumor in all directions. They reported that it was attached to the muscle cone. This is in spite of the fact that I could feel or see no attachment to the cone of the original tumor.

"Before exenteration comprehensive roentgenograms were taken, and no evidence of distant metastasis was found. The orbit is granulating well, and as late as April 14, 1941 no sign of local periorbital recurrent growth has been noted."

Microscopic Examination.—Primary Tumor (fig. 8): The tumor consisted of masses of small round or slightly spindle-shaped cells with scanty basophilic cytoplasm which frequently was vacuolated. The nuclei were small and round and stained deeply. The general appearance gave a first impression of ordinary round cell sarcoma. Close examination, however, disclosed among the aforementioned cells numerous larger ribbon-shaped cells with strongly acidophilic cytoplasm and nuclei which were small, dark and indistinct in the preparations available. The cytoplasm occasionally contained longitudinal fibrillation, and diligent search finally revealed definite cross striation in several instances with the Masson stain. No definite mitoses were seen. There were a few large, round, pink-staining cells with multiple nuclei.

Recurrence: A specimen of the recurrent tumor removed at exenteration on March 26 showed essentially the same picture with the exception that in certain areas the cells were more spindle shaped and the pink-staining ribbon cells fewer. Lack of additional sections precluded further differential staining and more careful study.

Comment.—In this case the diagnosis was more difficult, since the resemblance to muscle tissue of the most numerous cells was not readily apparent. Only close inspection, disclosing the less frequent scattered tumor cells with definite cross striation, proved the muscle tissue origin.

CASE 5.—L. C., a 13 year old boy, in 1933, at the age of 5½ years, was discovered to have bilateral retinoblastoma, more advanced in the left eye. After enucleation of the left eye, in which the diagnosis was proved histologically, he was given divided doses of roentgen therapy to the right orbit. Between Sept. 29, 1933 and April 15, 1935 he received a total of 13,046 r to the right temporal region and a total of 11,424 r to the right inner canthus and the left side of the bridge of the nose, the rays having been directed toward the posterior portion of the globe. Regression of the retinal tumor was satisfactory. In February 1940 the patient had a radiation cataract extracted, after which there was still no evidence of activity of the retinal growth.

In November the parents began to notice slowly progressive prominence of the right eye and the patient complained of impaired vision. Examination on Jan. 3, 1941 revealed a corrected vision of 15/200 and moderate diffuse conjunctival injection; an exophthalmometer reading was 29 (fig. 9). The cornea showed no evidence of exposure, and the fundus was well seen, showing moderate papilledema and hard white deposits in the macula. No mass was palpable in the orbit. Roentgenograms disclosed a defect in the lateral wall of the orbit, with destruction of bone. Examination of the left socket showed the gold ball implantation not to lie in the muscle funnel but to be dislocated up and out just beneath the conjunctiva. No mass was palpable in the left orbit. Neurologic examination revealed a slight left-sided coordination defect in addition to an increase in the deep reflexes on the left and a positive Babinski sign on this side.

Fig. 9 (case 5).—Photograph taken Jan. 4, 1941, just prior to exploration of the right orbit, showing exophthalmos of the right eye.

On January 10 the right orbit was explored through the external canthus, and a large amount of soft yellowish gray tumor tissue was found to fill it.

Since February 20 the patient has been receiving roentgen treatment in doses of 500 r every two days to the right supraorbital and infraorbital regions. There has been some regression of the exophthalmos, but a soft moundlike swelling has appeared in the right temporal region above the zygoma. Aspiration biopsy of this lesion showed bloody fluid without definite evidence of tumor.

Microscopic Examination (fig. 10).—The specimen was somewhat distorted by hemorrhage. The tumor was composed of large cells of all shapes arranged in an irregular manner. Striking were the nuclei, which were usually large, oval,

deeply staining, frequently multiple and lobulated and contained finely granular chromatin and one or more nucleoli. There were also small round nuclei occurring either in cells with additional larger nuclei or lying free between the cells. The cell outlines were indistinct. The cytoplasm was abundant, moderately acidophilic, frequently granular and vacuolated. There were many giant cells with monstrous nuclei. Mitoses were fairly common. In many areas there was a pink-staining mucinous fluid between the cells. The phosphotungstic acid–hematoxylin stain revealed occasional myofibrils in the cytoplasm of some of the cells.

Fig. 10 (case 5).—Section of the tumor tissue removed at exploration (hematoxylin and eosin stain; × 360).

Comment.—The determining features in this case were the great polymorphism of the cells, the frequency of vacuolated and granular cytoplasm, the presence of monstrous nuclei and the presence of myofibrils in the cytoplasm of some of the cells. From the histologic and clinical evidence there is little to support the natural first assumption that the tumor was related in some way to retinoblastoma. Indeed, the tumor resembled microscopically the rhabdomyosarcoma produced by Haagensen and Krehbiel in animals by injection of 1,2,5,6-dibenzanthracene. Haagensen, in a communication to us, stated the belief that the tumor may have been induced by the irradiation which had been

instituted seven and a half years previously. Such an occurrence elsewhere in the body is not unknown.

SUMMARY OF CASES

By way of summarizing the main features of the cases appearing in the literature and of those reported by us, there follows a brief comparative analysis:

Age.—On the basis of these two series of cases, rhabdomyosarcoma of the orbit may be said to be a tumor appearing most frequently in early childhood. For 13 of the cases reported in the literature, Pupo's case of a 70 year old woman being excluded, the average age at onset of symptoms was 6 years. That in the present series was 7 years if case 5 (age of onset 13), in which the tumor was probably not spontaneous, is included.

This average age corresponds to the age in most cases of sarcoma of the orbit and of perineal rhabdomyosarcoma, which also occurs in children, but it does not correspond to the average age in most cases of rhabdomyosarcoma of the skeletal musculature, which usually occurs in adults past 40.

Sex.—There appears to be a tendency for rhabdomyosarcoma of the orbit to occur in males more often than in females. Of the 14 previously reported cases, the patient was male in 8 and female in 4; in 2 cases the sex of the patient was not given. In the present series there were 4 males and 1 female. The totals for the two series were thus 12 males and 5 females.

Location.—The right side was involved a little more frequently than the left. In 4 of the previously reported cases the side was not mentioned. Of the remaining 10 cases, the right orbit was involved in 7 and the left in 3. Of the present series, the right orbit was involved in 2 cases and the left in 3.

There appears to be a tendency for the primary tumor to appear at the upper-inner portion of the orbit. Of the previously reported cases the location of the original tumor was not mentioned in 3 and was first apparent in the upper portion of the orbit (most frequently at the inner aspect) in 9 and below the globe in 2. Of the present cases, the tumor appeared first above the globe in 2 (in 1 at the inner aspect and in 1 at the outer aspect) and below the globe in 2 (in 1 nasally and in 1 temporally) and in 1 (case 5) was retrobulbar and diffuse.

Course.—Of the previously reported cases the final outcome was stated in only 5, although in another there were signs and symptoms of generalized metastases when the patient was last seen. Except Pupo's patient, a 70 year old woman who died of bronchopneumonia two months after excision of the tumor, all 5 patients died of metastases without showing any involvement of regional lymph nodes. In 4 of the cases in

which the duration of life after discovery of the tumor was given it averaged one year and five months. An arrest of the growth was reported in only 1 instance: Dérer's case, in which there had been no recurrence two and half years after exenteration.

Of the patients in the present series, patient 1 is living and well, without signs of local or general recurrence, exactly two years after exenteration of the orbit and three years after discovery of the tumor. Patient 2 is likewise well and shows no recurrence exactly two years after exenteration of the orbit and three and a half years after the first appearance of the tumor. Patient 3, with a large, rapidly growing tumor, died five months after exenteration of the orbit and six months after the first symptoms appeared. Patient 4 is well and without signs of recurrence one month after exenteration and six months after the first appearance of the tumor. Patient 5, with evidence of local extension of the tumor, is at present receiving intensive irradiation, but of course the prognosis is poor.

Treatment.—As in the treatment of other malignant tumors, attempts at local excision are usually followed by recurrence. Of the previously reported cases, exenteration of the orbit was performed in 5. In 2 of these there was a recurrence, in 1 there had been no recurrence after two and a half years and in the remaining 2 no follow-up was reported.

As previously mentioned, irradiation is not effective in the treatment of rhabdomyosarcoma elsewhere in the body. Some form of radiotherapy is mentioned as having been given in 4 of the cases of rhabdomyosarcoma previously reported. In the case of Enriquez it "produced no change." In the case of Monbrun and Offret a recurrent tumor regressed for two months after radium needles had been implanted and left for nine days but then recurred. In the case reported by Castren and Teräskeli "the last recurrence was not influenced by radium." Sjögren mentioned no improvement in his case after roentgen therapy.

In our own series all patients have received varying amounts of radiation at the Memorial Hospital for the Treatment of Cancer and Allied Diseases. In case 1 a total of 3,600 r was given after the second recurrence but there was another recurrence in three months. Case 2 was unusual in that after a total of 3,600 r there was apparent complete clinical regression of the primary tumor for fifteen months. The recurrent tumor which then developed was totally insensitive to an additional 2,750 r. In case 3 the first recurrent tumor after exenteration was treated with a total of 3,000 r but continued to progress, as did the next recurrence, which was treated by the implantation of radon seeds in the orbit. In case 4 a total of 6,000 r was given to the region from which the primary tumor had been removed but a recurrent tumor promptly developed. In case 5 roentgen therapy is at present being given to the right orbit and there has been some decrease in the amount of exophthalmos.

It is clear, therefore, that, although in 1 instance there was temporary clinical regression for a period of fifteen months, rhabdomyosarcoma of the orbit is generally unaffected by irradiation.

Histologic Aspects.—In all the previously reported cases except that of Redslob the author has been able to demonstrate tumor cells containing longitudinal and transverse striations. The inability of Redslob to find cross striations in his tumor does not in itself remove his case from the group.

It is significant that in three reports, those of Redslob, Sjögren and Castren and Teräskeli, the authors stressed the fact that the recurrent tumor had the appearance of "round cell sarcoma."

Autopsy was performed in only 1 previously reported case, that of Haythorn and Heckel, who, interestingly enough, were able to demonstrate striation in the tumor cells of the metastasis in the lung.

COMMENT

There is a tendency to call some malignant tumors of the orbit "sarcoma" with no further designation than "round cell" or "anaplastic." It is probable that not infrequently some of these tumors under the proper conditions of study could be identified as rhabdomyosarcoma. For this purpose it is essential to have the tissue well fixed immediately on removal, preferably in Zenker's solution. The sections should be no thicker than 5 microns, and the differential stains of Van Gieson and Masson and phosphotungstic acid–hematoxylin stain should be employed.

Burgess, in reference to tumors elsewhere in the body, said it was likely that many tumors in musculature going under the name of sarcoma, alveolar sarcoma, large cell round cell sarcoma, etc., are really rhabdomyosarcoma. Masson, Montpellier and Abrikossoff, furthermore, have stated that many tumors thought to be connective tissue sarcoma are of muscular origin (Jönsson). In describing 2 cases of rhabdomyosarcoma of the extremities, MacCallum stated:

> The ease with which the special features of the group are detected varies considerably with the specimen, and since the criterion frequently demanded before an origin from muscular tissue will be admitted is the demonstration of the characteristic cross striations, it is not at all improbable, indeed is almost certain, that many tumors truly of such origin or character are not recognized as such, and are relegated to the tumor scrap-heap of sarcoma.

In relation to rhabdomyosarcoma of the orbit, views similar to MacCallum's were expressed by Redslob, López Enriquez, Mier, Pupo, Sjögren and Mawas. They are plausible when it is considered that in three reports, those of Redslob, Sjögren and Castren and Teräskeli, the authors stated that without knowledge of the previous specimens the character of the cells of the recurrent tumors would have led to the diagnosis of round cell sarcoma. This may also be said of the third recurrence in case 1 and of the distant metastases in case 3 in our series.

Cappell and Montgomery stated for rhabdomyosarcoma in general that primary tumors in which striations are prominent may give rise to extremely anaplastic round cell metastases.

In a series of 14 cases of sarcoma of the orbit of all types, studied by Reese in 1934, in which the average age was 10 years, it was found that the average duration of life of the 12 patients who could be traced was only one year regardless of the type of treatment.

Because of the note of pessimism sounded by most writers as to the ultimate prognosis of sarcoma of the orbit in children, we feel that the recognition of rhabdomyosarcoma may be important in providing a more hopeful outlook, since exenteration of the orbit has in 2 cases resulted in no signs of recurrence after two years.

SUMMARY

The subject of rhabdomyosarcoma of the orbit is reviewed and 14 well defined cases collected from the literature. With 1 exception the patients were young children, and the course was characterized clinically by rapid growth of the tumor and, in the 5 cases followed, death of the patient within one and a half years after appearance of the tumor. In only 1 case in the series was the growth said to have been arrested for any length of time, and that was the case of Dérer in which there had been no recurrence two and a half years after exenteration.

Five additional cases which we studied personally are reported. All 5 patients received preliminary irradiation, and this was without effect on the growth except in patient 2, in whom there was temporary clinical regression for fifteen months. Of the 5 patients, 2 are without evidence of recurrence two years after exenteration of the orbit and more than three years after the first appearance of the tumor. One patient is without evidence of recurrence one month after exenteration of the orbit. One patient died five months after exenteration of the orbit. In 1 patient the tumor developed behind the remaining eye after enucleation of one eye and intensive irradiation to the other for bilateral retinoblastoma seven years previously, suggesting that it may have been induced by irradiation.

The apparent arrest of the growth in 2 cases suggests to us that this type of orbital sarcoma has a more favorable prognosis than that generally assumed for sarcoma of the orbit in general.

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CONTROL OF PAIN IN ACUTE IRIDOCYCLITIS WITH ISOAMYLHYDROCUPREINE

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The pains which may occur in acute iridocyclitis are among the most severe to which mankind may be subjected. It is often impossible to control them satisfactorily even with morphine or codeine, and the unfortunate patient must be allowed to suffer some twenty-four to forty-eight hours after vigorous treatment has been instituted.

In acute iridocyclitis the pain is a spasmodic ciliary neuralgia superimposed on a dull ache and is worst in the acute stages, when the tissue is swollen and hyperemic and the nerve endings are stimulated by a high concentration of toxic substances.[1] This pain is not confined to the eye but usually radiates over certain divisions of the trigeminal (the fifth) nerve. The malar region and the cheek may be involved, but by far the commonest site of radiation is the brow and the forehead via the supraorbital nerve. This neuralgia-like pain bears no definite relation to the severity of the inflammation but in intensity apparently keeps pace with the photophobia and the secretion of tears, as it obviously should do since all three are excited by irritation of the trigeminal nerve.

In an attempt to control this pain it was first found that relief for several hours could frequently be obtained by infiltrating the region of the supraorbital nerve with procaine hydrochloride; after this, in an effort to secure prolonged analgesia, isoamylhydrocupreine dihydrochloride (eucupin-hydrochloride) was used. The results in twenty-two cases of severe pain in the past two years have been almost uniformly good; the most severe component of the pain was relieved for from twenty-four to forty-eight hours, after which the condition was usually well enough controlled that pain had become a factor of less importance.

Isoamylhydrocupreine dihydrochloride is a drug well known to both proctologists and otolaryngologists; combined with 1 per cent procaine hydrochloride it has been shown to give satisfactory prolonged surgical anesthesia after rectal operations.[2]

From the Department of Ophthalmology, Baylor University School of Medicine.

1. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 2199.

2. Kilbourne, N. J.: Local Anesthetics Producing Prolonged Analgesia: Elimination of Pain After Rectal Operations, Surg., Gynec. & Obst. **62**:590-604 (March) 1936.

Morrison,[3] Laszlo and Hauck[4] and others have shown conclusively that this drug is most efficient in producing prolonged analgesia after tonsillectomy when used as an infiltration anesthetic.

Isoamylhydrocupreine is an almost tasteless white powder closely related to quinine. It is soluble in alcohol, ether, chloroform and hot vegetable and animal oils and fats but insoluble in water. The dihydrochloride has a very bitter taste, is soluble in fifteen parts of water and is easily soluble in alcohol. It is precipitated by alkalis.

Morgenroth and Bumke[5] showed the drug to have bactericidal powers, killing streptococci in 1:4,000 dilution and Staphylococcus aureus in 1:800 dilution, and to be bacteriostatic to Staph. aureus in 1:160,000 dilution.

The pharmacologic action of isoamylhydrocupreine is similar to that of quinine; large doses given to animals stimulate the vagus nerve and the respiratory centers in the medulla. The drug is mainly inhibitory on smooth muscle, causing relaxation. The pressor effect of epinephrine is diminished by isoamylhydrocupreine; so when the latter is used as a local anesthetic more epinephrine must be added to diminish the hemorrhage. Direct application of isoamylhydrocupreine in 1:1,000 solution paralyzes sensory nerve fibers. The local anesthetic action of the drug is marked but the onset delayed because of slow diffusion in tissue.[6] For this reason, and because injections cause some initial burning sensation, it is customary to employ the drug in combination with procaine hydrochloride.

The toxicity of the drug has been shown to be relatively low, de Takáts[7] having demonstrated that none of the usual injections of isoamylhydrocupreine dihydrochloride in isotonic solution cause any local irritation. The use of watery solutions has been followed by sloughing, and solutions stronger than 0.2 per cent may cause local reactions. Kilbourne[2] found the minimum lethal dose to be 150 mg. per kilogram of body weight, which is one-tenth that of nupercaine though twice that of procaine hydrochloride.

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3. Morrison, W.: A Short Report on the Use of a New Anesthetic Agent Which Gives Prolonged Analgesia, Laryngoscope **48**:272-275 (April) 1938.

4. Laszlo, A. F., and Hauck, R. F.: Prolonged Post-Operative Anesthesia in Tonsillectomy, Ann. Otol., Rhin. & Laryng. **47**:527-530 (June) 1938.

5. Morgenroth, J., and Bumke, E.: Zur chemotherapeutischen Desinfektion durch Chinaalkaloide und ihre Abkömmlinge, Deutsche med. Wchnschr. **44**:729-733, 1918.

6. Bylsma, U. G.: Die pharmakologische Wirkung von Vuzin und Eukupin, Ztschr. f. d. ges. exper. Med. **11**:257, 1920-1921.

7. de Takáts, G.: Prolongation of Local Anesthesia, Surg., Gynec. & Obst. **43**:100, 1926.

That idiosyncrasy is of extreme rarity has been demonstrated by Dawson and Garbade,[8] although repeated injections may cause its development. In over 300 cases of tonsillectomy Laszlo and Hauck[4] observed no evidence of sensitivity; however, urticaria following injection of the drug has been reported, as well as a case of widespread erythema without pruritis.[3]

In the group of cases under present discussion an effort was made to inject the drug at the site of the supraorbital nerve just as it leaves the orbit through the supraorbital notch. Important anatomic points to remember in this connection are: first, that the supraorbital nerve usually divides on the forehead, but sometimes within the orbit, into a medial and a lateral branch, and, secondly, that the supraorbital notch is bridged over by a periosteal ligament which ossifies in 25 per cent of cases, converting the notch into a foramen or even into a canal 5 to 15 mm. long.[1] A 1:500 concentration of isoamylhydrocupreine dihydrochloride in 1 per cent solution of procaine hydrochloride was used with 8 minims (0.5 cc.) of epinephrine added to the ounce (30 cc.) to minimize the danger of formation of hematoma. An average of 0.5 cc. of this mixture being used, the severe supraorbital pain was completely abolished in 19 of 22 cases for a period of from twenty-four to forty-eight hours, after which pain in the region was relatively mild. In 3 cases there was definite lessening of pain over the brow, although complete analgesia was not obtained. The effect of the drug was dissipated in less than twenty-four hours, and the results were attributed to either a poor injection or pronounced anatomic irregularities. In spite of its close anatomic association with the supraorbital nerve, the supratrochlear nerve did not seem to be involved to a commensurate degree, and it was not directly injected.

The only undesirable development noted was the frequent occurrence of edema involving the upper lid twelve to twenty-four hours after the injection; however, this was moderate and not really troublesome, usually disappearing in from twenty-four to forty-eight hours.

SUMMARY

Twenty-two patients with acute iridocyclitis in which supraorbital pain was a prominent feature were treated by injecting the region of the supraorbital nerve with a solution of isoamylhydrocupreine dihydrochloride and procaine hydrochloride solution to which epinephrine had been added. The larger component of the patients' pain was removed for from twenty-four to forty-eight hours, the freedom from severe pain allowing time for vigorous treatment to control the initial ravages of the condition while the patient remained in comparative comfort.

8. Dawson, W. T., and Garbade, F. A.: Idiosyncrasy to Quinine, Cinchonidine and Ethylhydrocupreine and Other Levorotatory Alkaloids of the Cinchona Series: Preliminary Report, J. A. M. A. **92**:704-705 (March 8) 1930.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

MUSTARD GAS INJURIES TO THE EYES

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OUTLINE

I. Incidence
II. Dose necessary to produce lesion
III. Course of severe corneal burns
IV. Action on tissue
  A. Local Action
    1. Liberation of hydrochloric acid
    2. Derivatives
    3. Whole molecule
    4. Tissue hypersensitivity
  B. Systemic Action
    1. Break-down products
    2. Metabolism
    3. Bone marrow
    4. Antibodies
    5. Changes secondary to burns
    6. Fundus changes
V. Prophylaxis
VI. Treatment
  A. Patients without corneal involvement
    1. Reassurance
    2. Irrigations
      (*a*) Bland solutions
      (*b*) Hypertonic solutions
      (*c*) Neutralizing agents
      (*d*) Irrigating apparatus
    3. Dark glasses or eye shade
    4. Convalescence
  B. Patients with corneal involvement
    1. Immediate treatment
    2. Oily drops and ointments
    3. Ascorbic acid
    4. Secondary infections
      (*a*) Mild silver protein and boric acid
      (*b*) Antiseptics
      (*c*) Sulfanilamide and derivatives
    5. Convalescence
    6. Late treatment
VII. Summary of present treatment

From the Wilmer Ophthalmological Institute of Johns Hopkins University and Hospital.

I. INCIDENCE

The present treatment of mustard gas—dichlorodiethylsulfide, or $(ClCH_2CH_2)_2S$—injuries to the eyes is largely derived from the methods developed during the first World War. The incidence of mustard gas injuries during that period, with the clinical and the pathologic characteristics, has been summarized in the "Official History of the War." [1] It was found that 75 to 90 per cent of all mustard gas casualties presented some degree of ocular involvement. The patients were divided into three groups:

1. Those who showed only mild conjunctival irritation, representing about 75 per cent of the total. This reaction quickly subsided in one or two weeks with symptomatic treatment.

2. Those with severe conjunctival involvement, showing a horizontal band of white chemosis between the lids. The corneal surface might present an "orange peel" roughening but would not stain with fluorescein. These patients represented about 15 per cent of the total, and recovery took place after four to five weeks.

3. Those with corneal erosion, comprising about 10 per cent. This group demanded the attention of an ophthalmologist, and convalescence required two or three months.

Other reports of serious immediate complications show an amazingly low incidence. Teulières [2] reported on 1,500 mustard gas casualties, and only 23 presented ocular lesions severe enough to necessitate observation on a special service. Three showed ulceration of the cornea, and in 1 panophthalmitis developed. In a series of 1,800 mustard casualties, Beauvieux [3] found only 2 in whom severe corneal ulceration developed, and these ultimately recovered useful vision.

There are several reports [4] on patients in whom corneal ulceration recurred as long as seventeen years after the injury. All these patients

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1. History of the Great War, Based on Official Documents: Medical Services; Diseases of the War, London, His Majesty's Stationery Office, 1923, vol. 2, p. 425.

2. Teulières: Lésions oculo-palpébrales par nouveaux gaz, J. de méd. de Bordeaux **48**:37, 1918.

3. Beauvieux: Les lésions oculaires par gaz vésicants, Arch. d'opht. **37**:597, 1920.

4. Genet, L.: Ypérite, ischémie conjonctivale, ulcère cornéen tardif, Bull. Soc. d'opht. de Paris, 1937, p. 409; abstracted, Zentralbl. f. d. ges. Ophth. **40**: 41, 1937-1938. Heckford, F.: Delayed Corneal Ulceration Following Mustard Gas Burns, Proc. Roy. Soc. Med. **30**:949, 1937. Genet, L., and Delord, E.: Ypérite, kératite symétrique tardive à allure trophique, Bull. Soc. d'opht. de Paris, 1936, p. 521; abstracted, Zentralbl. f. d. ges. Ophth. **37**:685, 1937. Neame, H.: Late Result After Mustard Gas Burn of the Eyes, Proc. Roy. Soc. Med. **22**: 25, 1928. Jacqueau and Bujadoux: Infection aiguë et spontanée des deux globes oculaires, à deux ans d'intervalle, chez un ancien ypérite, Cong. Soc. franç. d'opht., Bruxelles, 1925; abstracted, Zentralbl. f. d. ges. Ophth. **16**:787, 1926.

had had severe corneal burns originally but were free of symptoms previous to the recurrence. Anesthesia of the cornea was not a prominent feature. Several authors stressed the occurrence of peculiar varices of the conjunctival vessels at the limbus. Symptoms of chronic conjunctival irritation with photophobia and mild recurrent corneal erosions in scarred areas may predominate, or devastating ulcerations may occur.

There are no statistical reports of the ultimate visual status of all patients in whom the cornea was involved originally. A small degree of visual loss may be the most common residual. If mustard gas is used in future aerial bombing, there will probably be a higher percentage of severe corneal injuries produced by splashing of the liquid.

The purpose of this review is to summarize the published information on the mechanism of action of mustard gas on living tissues and the present treatment of mustard gas injuries to the eyes.

II. DOSE NECESSARY TO PRODUCE LESION

Identical lesions can be produced in the eyes by the instillation of liquid mustard and by exposure to mustard vapor. Warthin and Weller [5] produced destructive corneal lesions by the instillation of 0.0004 cc. of liquid mustard, and this dose was also used by Mann and Pullinger [6] in their experiments on rabbits. Arnold [7] used 0.008 cc. and found that the darkly pigmented rabbits were the least sensitive. Pellathy [8] found that rabbits' eyes could withstand 0.2 to 0.4 mg. of liquid mustard when it was applied to the conjunctival fold with a platinum loop. Application of 1 mg. of mustard in this manner would destroy the cornea and the globe. Vejdovsky [9] found that pigs' eyes were more sensitive than the eyes of rabbits or of dogs. Wessely [10] found that the course of mustard vapor lesions in apes resembled that of such lesions in human beings.

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5. Warthin, A. S., and Weller, C. V.: The Medical Aspects of Mustard Gas Poisoning, St. Louis, C. V. Mosby Company, 1919; J. Lab. & Clin. Med. **4**:785, 1919.

6. Mann, I., and Pullinger, B. D.: Experiments on Effect of Ascorbic Acid in Mustard Gas Burns, Brit. J. Ophth. **24**:444, 1940.

7. Arnold, H.: Beiträge zur Pathologie der Augenschädigung durch Dichlordiäthysulfid auf Grund von Tierversuchen, Thesis, Berlin, 1937; abstracted, Zentralbl. f. d. ges. Ophth. **40**:42, 1937.

8. Pellathy, B.: Versuche zur Ermaszigung der Wirkung des Senfgases, Klin. Monatsbl. f. Augenh. **98**:688, 1937.

9. Vejdovsky, V.: Die Wirkung flüssigen Yperits auf die Augen einiger Tiere, Českoslov. ofth. **3**:169, 1937; abstracted, Zentralbl. f. d. ges. Ophth. **40**: 554, 1937-1938.

10. Wessely: Ueber die Wirkung des Dichloräthylsulfids auf das Auge, Klin. Monatsbl. f. Augenh. **94**:100, 1935.

The severity of ocular lesions produced by mustard vapor is dependent on the concentration of the vapor and the length of exposure. The action of mustard vapor is accumulative, both for the skin and for the eyes. Eyester and Maver [11] found the minimal concentration of vapor necessary to produce an ocular lesion in the rabbit after thirty minutes' exposure to be 0.07 mg. per liter. Reed [12] produced a definite conjunctivitis in dogs by two hours' exposure to a concentration of 0.001 mg. per liter. Exposure for only one hour to this concentration produced no irritation. After testing the eyes of fourteen human beings whose cutaneous resistance was relatively high, Reed found that visible reactions were produced in less than one hour of exposure to the concentration of 0.0005 mg. per liter of air (1 part in 10,000,000). As compared with the skin, he found that the eyes reacted to much lower concentrations of mustard vapor.

III. COURSE OF SEVERE CORNEAL BURNS

The clinical and the pathologic course of severe mustard gas lesions of the cornea in the rabbit [13] and in man [14] have been well described. There are several well recognized stages:

1. Immediate damage to the corneal epithelium with edematous clouding and necrosis of the stroma.

2. After five hours, an infiltration of polymorphonuclear cells at the sclerocorneal junction, thence extending into the corneal stroma.

3. Clinical improvement of the opacity after five to seven days, with diminished edema of the stroma.

4. Progressive vascularization of the cornea extending in from the limbal vessels. This process may continue for several weeks.

5. Persistent ulceration of the cornea for weeks or recurrent ulceration after a latent period of years.

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11. Eyester, J., and Maver, M.: An Apparatus for the Exposure of Skin or Mucous Membrane to the Vapor of Toxic Substances, with Observations on Dichlorethylsulphide, J. Pharmacol. & Exper. Therap. **15**:95, 1920.

12. Reed, C. I.: The Minimum Concentration of Mustard Gas Effective for the Eyes of Man, J. Pharmacol. & Exper. Therap. **15**:77, 1920.

13. Livingston, P. C., and Walker, H. M.: Effects of Liquid Mustard Gas upon Eyes of Rabbits and of Certain Methods of Treatment, Brit. J. Ophth. **24**: 67, 1940. Warthin and Weller.[5] Mann and Pullinger.[6]

14. Poole, L. T.: Chemical Warfare in Relation to Ophthalmology, in Ridley, F., and Sorsby, A.: Modern Trends in Ophthalmology, London, Butterworth & Co., Ltd., 1940, p. 636. History of the Great War, Based on Official Documents: Medical Services; Surgery of the War, London, His Majesty's Stationery Office, 1922, vol. 2, p. 530. Footnote 1. Warthin and Weller.[5]

IV. ACTION ON TISSUE

A. *Local Action.*—Warthin and Weller [5] showed that the postmortem application of liquid mustard to the cornea produced no histologic lesions which could be attributed to the action of mustard. The mechanism of the action on living tissues is not clear, and many theories have been developed.

1. Liberation of Hydrochloric Acid: Lynch, Smith and Marshall [15] produced evidence which they stated indicates that the toxic action of mustard is due to an intracellular liberation of hydrochloric acid by hydrolysis:

$$(ClCH_2CH_2)_2S + 2HOH \rightarrow (HOCH_2CH_2)_2S + 2HCl$$

They found that similar lipid-soluble substances, monochlorodiethylsulfide and the two isomeric dichlorodipropylsulfides, also hydrolyze readily with the production of hydrochloric acid. These related substances are somewhat irritating to the skin and the lungs. The authors suggested that reduced temperature may lower the hydrolysis and toxicity of mustard in a manner similar to the reduction of the toxicity of atoxyl (reduced in the body) and colchicine (oxidized in the body) in frogs which are kept at low temperatures. They found that catfish and goldfish survived a half-saturated solution of mustard at 10 C. for ten minutes but were killed when the temperature was kept at 25 C. However, catfish can survive three to fifteen times the concentration of hydrochloric acid theoretically formed by the hydrolysis of a half-saturated solution of mustard. The authors stated that lipid solubility is a prerequisite for the penetration and intracellular liberation of the acid. Marshall and Williams [16] also pointed out that the oxidation product, dichlorodiethylsulfone, or $(ClCH_2CH_2)_2SO_2$, which they stated hydrolyzes readily, is toxic for human skin and for the protoplasm of the paramecium. On the other hand, dichlorodiethylsulfoxide, $(ClCH_2CH_2)_2SO$, does not hydrolyze readily in weak alkali and is not toxic for the skin or for the paramecium. Lillie, Clowes and Chambers [17] demonstrated that mustard retards and deforms normal cell division of fertilized starfish eggs after a short latent period of three or four normal cell divisions. The hydrolytic product, dihydroxydiethylsulfide, or

15. Lynch, V.; Smith, H. W., and Marshall, E. K., Jr.: Systemic Effects and Mechanism of Action of Mustard Gas, J. Pharmacol. & Exper. Therap. **12**:265, 1918.

16. Marshall, E. K., Jr., and Williams, J. W.: The Toxicity and Skin Irritant Effect of Certain Derivatives of Dichloroethylsulfide, J. Pharmacol. & Exper. Therap. **16**:259, 1920.

17. Lillie, R. S.; Clowes, G. H. A., and Chambers, R.: Penetration of Mustard Gas into Marine Organisms, and the Mechanism of Its Destructive Action on Protoplasm, J. Pharmacol. & Exper. Therap. **14**:75, 1919.

$(HOCH_2CH_2)_2S$, is nontoxic, whereas an equivalent amount of hydrochloric acid injected into the cell produces damage similar to that produced by injected mustard, except that there is no latent period. Previous treatment of Arenicola larvae with weak aniline, ammonia or ethyl alcohol, will protect them against mustard and other injurious agents. This protection is thought to be due to the "anesthetic" properties of these solutions and not to the neutralization of any hydrochloric acid which may be formed. Addition of neutral red to starfish eggs which are intoxicated with mustard will demonstrate the accumulation of acid granules. This is not the case if neutral red is added before mustard.

Erdmann [18] found that the vapor of dimethylsulfate, $(CH_2O)_2SO_2$, will produce a violent corrosive burn of the cornea. He noted that there was a close relation between the integrity of the endothelium and the development or subsidence of corneal edema. Lynch, Smith and Marshall [15] suggested that the production of sulfuric acid by hydrolysis may be the underlying cause of the toxicity of dimethylsulfate for the endothelium.

There is much evidence against the view that mustard is toxic because of its intracellular acid production. Attempts to neutralize the destructive effect of mustard by the injection of alkaline substances have failed. Peters and Walker,[19] using titration methods in vitro, found that the rates of acid liberation in 5 per cent alcoholic solution were: dichlorodimethylsulfide 500, dichlorodiethylsulfide (mustard gas) 100, tetrachlorodiethylsulfide 4, hexachlorodiethylsulfide 1, dichlorodiethylsulfone 1, trichlorodiethylsulfide 0. Since only mustard gas and dichlorodiethylsulfone are vesicants, there is no in vitro evidence of a relation between rates of hydrolysis and the vesicant property. All these substances have similar lipid solubility. Kamm and Waldo [20] found no vesicant properties in dichlorodiethylether, a substance which has an oxygen atom instead of the sulfur atom of mustard gas.

Although the acid theory of mustard toxicity has not been established, the tolerance of the cornea for the theoretic quantity of hydrochloric acid from mustard hydrolysis has not been determined. Clinically, mustard burns of the cornea resemble alkali burns more than acid burns.

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18. Erdmann, P.: Ueber Augenveränderungen durch Dimethylsulfat, Arch. f. Augenh. **62**:178, 1909.

19. Peters, R. A., and Walker, E.: Rate of Liberation of Acid by Mustard Gas and Its Analogues in Its Relation to the "Acid" Theory of Skin Vesication, Biochem. J. **17**:260, 1923.

20. Kamm, O., and Waldo, J. H.: B-B′ Dichlorodiethyl Ether: The Oxygen Analogue of Mustard Gas, J. Am. Chem. Soc. **43**:2223, 1921.

2. Derivatives: Flury and Wieland [21] suggested that an oxidative derivative of mustard may be a more stable and irritating substance; e. g., dichlorodiethylsulfone $(ClCH_2CH_2)_2SO_2$, possibly formed by the action of skin oxidases on mustard. This is unlikely because mustard gas itself is more toxic than the sulfone and another oxidation product, dichlorodiethylsulfoxide $(ClCH_2CH_2)_2SO$, is nonvesicant. Lynch, Smith and Marshall [15] found no material in mustard-produced cutaneous vesicles which would produce a toxic reaction in dogs when given intravenously.

Livingston and Walker [13] were unable to transfer to a normal eye by means of a platinum loop any toxic material from an eye in which 0.075 cc. of liquid mustard had been instilled fifteen minutes previously. If this is an adequate method for transfer of any residual mustard, it appears that the ocular secretions or tissues neutralized a drop of mustard within fifteen minutes. Merkulov [22] instilled 5 drops of a 1 per cent solution of mustard in petrolatum oil into a rabbit's eye. Fifteen minutes later the aqueous in this eye was found to be irritating to the conjunctiva of a normal eye.

3. Whole Molecule: In view of the conflicting evidence relative to the formation of toxic hydrolytic or oxidative products from mustard, Vedder [23] concluded that the immediate action of mustard is due to the whole molecule and that it is a "cell poison, exerting its necrotizing action on all cells with which it comes directly into contact, including the skin and mucous membranes with all their structures. The capillaries and other organs that mustard reaches become paralyzed." This view received support from the chemical investigations of Lawson and Reid.[24] They found that B,B'-dichloroethylsulfide (mustard) and its sulfone and the sulfoxide derivatives combine in vitro with various primary, secondary and tertiary amines. The resulting thiazane ring compounds (e. g. $RN<(CH_2CH_2)_2>S$) and other condensation products are nonvesicant, but Lawson and Reid's studies indicate the possibility that mustard may combine with tissue proteins directly.

4. Tissue Hypersensitivity: Tissue which has been the site of a mustard burn is susceptible to smaller concentrations of the vapor.

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21. Flury, F., and Wieland, H.: Ueber Kampfgasvergiftungen: VII. Die pharmakologische Wirkung des Dichloräthylsulfids, Ztschr. f. d. ges. exper. Med. **13**: 367, 1921.

22. Merkulov, I.: Therapeutische Behandlung bei Augenentzündung durch Yperit, Arch. oftal. **8**:97, 1931; abstracted, Zentralbl. f. d. ges. Ophth. **26**:152, 1932.

23. Vedder, E. B.: The Medical Aspects of Chemical Warfare, Baltimore, Williams & Wilkins Company, 1925.

24. Lawson, W. E., and Reid, E. E.: Reactions of Bb'-Dichloroethylsulfide with Amino Compounds, J. Am. Chem. Soc. **47**:2821, 1925.

Sollmann,[25] after testing a few persons for sensitivity of the skin to mustard, concluded that "healed mustard burns are oversusceptible to injury, mechanical or chemical, and therefore incidentally to mustard. Prolonged work with mustard and severe and extensive burns of the skin do not render the uninjured areas of the skin hypersensitive to mustard." On the other hand, Berenblum and Wormall [26] have immunized rabbits with intraperitoneal injections of horse serum treated with mustard. Positive precipitin and complement fixation reactions were obtained on the blood of these rabbits, mustard-treated rabbit serum being used as an antigen. The large amount of tissue necrosis in mustard poisoning may provide fertile ground for the formation of an antigenic mustard-protein combination, but the sensitization of normal skin has not been demonstrated.

B. *Systemic Action.*—1. Break-Down Products: After the application of mustard gas locally, nontoxic dihydroxydiethylsulfide, $(HOCH_2CH_2)_2S$, is found in the urine along with crystalline phenol and thiophenol condensation products. There is no evidence that any oxidation products or unsaturated vinyl groups ($CH_2{=}CH{-}$) are formed in the body and excreted in the urine. Lynch, Smith and Marshall [15] found no toxic material in blood taken from a dog during the convulsions which followed the intravenous injection of mustard. However, they found that the intravenous injection of 6 mg. per kilogram was fatal for dogs. The animals had salivation, diarrhea, tonic and clonic convulsions and a slow and irregular cardiac action followed by a rapid pulse and stimulation of respiration. Autopsies showed congestion and hemorrhages in the gastrointestinal tract, congestion of the lungs and variable congestion of the kidneys. Intravenous injections of large quantities of sodium bicarbonate solution somewhat alleviated the convulsions in these animals but did not prevent death.

2. Metabolism: Berenblum, Kendal and Orr [27] found that mustard, the sulfone derivative and cantharidin (which has no structural relation to mustard but is also a cutaneous irritant), which inhibit the induction of tar tumors, reduced the glycolysis of minced Jensen sarcoma 84 per cent and its respiration 50 per cent. On the other hand, the sulfoxide of mustard, dihydroxydiethylsulfide and croton oil, which have no inhibiting effect on carcinogenesis, did not reduce glycolysis more than respiration.

25. Sollmann, T.: The Question of Induced Hypersusceptibility of the Skin to Mustard Gas, J. Pharmacol. & Exper. Therap. **12**:319, 1918.

26. Berenblum, I., and Wormall, A.: Immunological Properties of Proteins Treated with Mustard Gas and BB'-Dichlorodiethyl Sulphone, Biochem. J. **33**:75, 1939.

27. Berenblum, I.; Kendal, L. P., and Orr, J. W.: Tumour Metabolism in Presence of Anti-Carcinogenic Substances, Biochem. J. **30**:709, 1936.

Jany and Sellei [28] found that mustard inhibited the aerobic glycolysis of Escherichia coli by 64 per cent, but the respiration was more than doubled. Peters [29] found that the sulfone of mustard inhibited the oxidation of pyruvate in brain tissue, although the change from lactic acid to pyruvate was not disturbed.

3. Bone Marrow: There is some evidence of a specific systemic toxic effect due to mustard when it is applied locally. Krumbhaar and Krumbhaar [30] studied 55 cases of fatal mustard poisoning at autopsy. The bone marrow showed areas of necrosis, less hyperplasia than is found in various acute inflammations and a predominance of immature cells. The picture resembled that of benzene poisoning. Pappenheimer and Vance [31] reported severe lesions in the bone marrow of rabbits which had been given a fatal dose of mustard intravenously, and this was associated with leukopenia. The blood of mustard gas casualties was studied by Krumbhaar,[32] and in the fatal cases and the next most serious cases he found initial leukocytosis followed by leukopenia. This finding has been confirmed in dogs by Hektoen and Corper,[33] who reported leukocyte counts up to 12,600 with a moderate shift to the left in the Arneth count between six to thirty-six hours after the injection of mustard. There was a progressive drop in the leukocyte count between the third and the fifth day to as low as 1,800, with a marked shift to the right (few immature cells).

4. Antibodies: Hektoen and Corper [33] were impressed by the similarity in action between benzene, roentgen rays, thorium X and mustard on the bone marrow. Since the first three substances inhibit the production of antibodies, the authors proceeded to demonstrate a delay in appearance of precipitins, a reduction and irregular production of lysins and a definite reduction of agglutinins after the administration of mustard to dogs.

5. Changes Secondary to Burns: Mustard gas casualties may show clinical and pathologic signs which are also seen secondary to heat burns

28. Jany, J., and Sellei, C.: Ueber die Wirkung einiger giftiger Gase auf den Stoffwechsel der Zelle, Biochem. Ztschr. **275**:234, 1935.

29. Peters, R. A.: Effect of Dichlordiethylsulphone on Brain Respiration, Nature, London **138**:327, 1936.

30. Krumbhaar, E. B., and Krumbhaar, H. D.: J. M. Research **40**:497, 1919; cited by Hektoen and Corper.[33]

31. Pappenheimer, A. M., and Vance, M.: Effects of Intravenous Injections of BB'-Dichlorodiethylsulfide in Rabbits, with Special Reference to Its Leucotoxic Action, J. Exper. Med. **31**:72, 1920.

32. Krumbhaar, E. B.: Role of the Blood and the Bone Marrow in Certain Forms of Gas Poisoning: Peripheral Blood Changes and Their Significance, J. A. M. A. **72**:39 (Jan. 4) 1919.

33. Hektoen, L., and Corper, H. J.: Effect of Mustard Gas on Antibody Formation, J. Infect. Dis. **28**:279, 1921.

of the skin, e. g. shock symptoms following loss of chlorides from the exposed areas, congestion and hemorrhages in the kidney and general toxemia associated with great damage to tissue.

6. Fundus Changes: Beauvieux [8] examined the fundi in 120 cases of severe generalized mustard gas lesions and noted venous dilatations in 34 per cent and hyperemia of the optic disk in 23 per cent. No cases of optic neuritis have been reported. Wessely [10] noted retinal hemorrhages only in those animal eyes which did not receive prophylactic ointment previous to the instillation of mustard. He concluded that such hemorrhages are probably due not to the general intoxication arriving via the blood stream but to the intoxication arriving via the burned ocular tissues.

V. PROPHYLAXIS

As pointed out, residual toxic material, e. g. mustard gas or other toxic compound, cannot be demonstrated in the external ocular secretions later than fifteen minutes after the instillation of liquid mustard. Since there is a latent period of two to forty-eight hours after the exposure to mustard vapor before the victim becomes aware of ocular symptoms, the initial necrotizing action is usually completed by the time the patient receives first aid treatment. There are as yet no fully satisfactory neutralizing agents which will be tolerated by the eye, and so prophylaxis becomes very important.

Poole [14] has summarized the methods of prophylaxis. As soon as the faint, transitory mustard or garlic odor is detected, or the presence of mustard gas is suspected, the gas mask should be adjusted immediately in order to prevent lesions of the eyes and the respiratory tract produced by the vapor. Liquid mustard will not penetrate glass. In addition to wearing gas masks when near any mustard fumes, the workers in English mustard factories irrigate their eyes several times a day with sodium bicarbonate or boric acid solution at convenient prophylactic stations. The oily secretion of the meibomian glands in the lids acts as a concentrating agent for mustard vapor, and repeated subminimal exposures result in an accumulative effect. The moist surfaces of the conjunctiva and cornea are also a factor in making the eye the most sensitive portion of the body toward mustard vapor. In field dressing stations, before the patients and their clothes have been decontaminated gas respirators should be worn by the attendants.

VI. TREATMENT

As noted, it has been estimated that about 75 per cent of all mustard gas casualties have some degree of ocular involvement. With respect to treatment and ultimate prognosis, these may be divided roughly into

those without corneal involvement (75 to 90 per cent of the cases) and those with corneal involvement. The conjunctival reaction may be severe without involvement of the cornea. There are no reports of cases in which the cornea showing no early damage underwent a late ulceration secondary to the conjunctival burn. Early corneal involvement manifests itself by a loss of luster and often an orange peel roughening of the surface, with diminished or absent corneal sensation. Warthin and Weller [6] showed in rabbits that ten minutes after the instillation of 0.0004 cc. of liquid mustard or exposure for fifteen minutes to 1:20,000 of the vapor, the cornea took punctate staining with 2 per cent fluorescein (alkaline aqueous solution). This corresponded histologically with pyknotic changes in the nuclei of the corneal epithelium before any erosion or ulceration had occurred. The degree of necrosis of the corneal epithelium corresponded closely with the depth of the staining with fluorescein. The patients with early corneal involvement are those in whom more serious complications may develop.

A. *Patients Without Corneal Involvement.*—1. Reassurance: Within two to forty-eight hours after contact with mustard, most patients show symptoms of marked conjunctivitis. The lids become greatly swollen, the conjunctiva becomes chemotic and there are marked photophobia, tearing and discharge. Often, therefore, the patient is unable to open his eyes and so fears that he is blind. This psychologic reaction may persist long after the patient has recovered from the physical effects of the mustard burn or may be the precipitating factor in the production of hysteria or "shell shock." For this reason the lids should be opened immediately to show the patient that his vision has not been lost.

Often the extreme chemosis of the lids and the photophobia make examination and treatment of the eyes very difficult. Local anesthetics should be avoided because they damage the corneal epithelium. Herrmann [34] has found that pontocaine inhibits the respiration of the beef cornea. Frequent instillations of any local anesthetic will produce staining of the corneal surface with fluorescein, and this is accentuated if the solution is hypotonic. There has been no experimental work reported on the comparison of the injurious effects of various local anesthetics which have equal anesthetizing properties. The use of cocaine is generally forbidden, but if necessary for the examination of the patient, 1 drop of isotonic pontocaine solution 0.5 per cent may be instilled.

2. Irrigations: Regardless of the facts that Livingston and Walker [13] could demonstrate no residual toxic material in the eye fifteen minutes after the instillation of liquid mustard and that irrigations five minutes

34. Herrmann, H.: Influence of Pontocaine Chloretone on the Respiration and Glycolysis of the Cornea, 1941, to be published.

after the instillation had no beneficial effect, irrigations are still offered as emergency treatment of mustard gas casualties as long as several hours after the exposure. To make the patient feel that something is being done for him and possibly to lessen the bacterial flora in the eye, such irrigations have value.

(*a*) Bland solutions: During the first World War both the Allies and Germany used the following solutions, evidently without any striking differences in therapeutic value being found among them: physiologic solution of sodium chloride, boric acid 2 per cent and sodium bicarbonate 1 or 2 per cent. Peters and Walker,[19] in titrating the hydrochloric acid formed from the hydrolysis of mustard, found no significant increase in the rate of hydrolysis when excessive alkali was added. One could therefore not expect a weak alkaline solution such as sodium bicarbonate 1.5 per cent, which is isotonic and has a p_H of 8.7, to have any hydrolytic effect on mustard during a short irrigation of the eye.

(*b*) Hypertonic solutions: Bonnefon[35] recommended the use of a hypertonic solution, such as saturated solution of sodium sulfate 800 Gm. with solution of dextrose 200 Gm. This, he stated, will increase the flow of tears and induce drainage from the tissues by osmosis. Dor[36] suggested the following hypertonic solution: magnesium sulfate 40 Gm., syrup of sugar (simple syrup) 50 Gm. and boiled water 150 cc.

(*c*) Neutralizing agents: Mustard can be rendered innocuous by hydrolysis, oxidation of the sulfur atom, chlorination or the formation of a condensation compound. A neutralizing substance must be obtained which will successfully attack mustard at a concentration which is tolerated by the eye.

The most successful neutralizing agent of this sort appears to be dichloramine-T in 0.5 per cent solution, which forms a nontoxic addition compound with mustard. Because of its relative insolubility in water, this substance must be dissolved in an organic solvent such as chlorinated paraffin or chlorinated diphenylether. Warthin and Weller[5] and Heinsius[37] reported a definite prophylactic effect in rabbits if this substance was used within fifteen minutes after the instillation of

35. Bonnefon: L'œil ypérité. Son traitement, Gaz. hebd. d. sc. méd. de Bordeaux **60**:168, 1939; Siècle méd., Sept. 1, 1939; cited in Gas Injuries to the Eyes, Special Articles, Lancet **2**:756, 1939.

36. Dor, L.: Gaz de combat et brûlures des yeux, Arch. d'opht. **3**:873, 1940.

37. Heinsius, E.: Experimentelle Untersuchungen über die Prophylaxe und Therapie der Gelbkreuzerkrankungen der Augen, in Heinsius, E.; Busch, H. G.; Stutz, E., and Reil, G.: Veröffentlichungen aus dem Gebiete des Marine-Samtätswesens, Berlin, Mittler, 1938; abstracted, Zentralbl. f. d. ges. Ophth. **43**:389, 1939.

mustard. A local anesthetic must be used before the irrigation with dichloramine-T in human beings. After the congestive effects produced by mustard have fully developed, the use of chlorinated solutions would probably increase the irritation without a significant reduction in the amount of residual toxic material.

The use of potassium permanganate in 0.4 to 1 per cent solution has shown no protective effect in rabbits.[38] As with most other neutralizing agents employed, there has evidently been no adequate determination of the tolerance of the normal eye for such strong solutions.

Trials with other neutralizing agents have been uniformly unsuccessful. Heinsius [37] and Pellathy [38] found no prophylactic effect with chloramine in 0.5 to 2 per cent aqueous solution. Pellathy found tannic acid in 1 to 10 per cent solution, acetic acid, chlorine-saturated carbon tetrachloride and powdered sodium sulfate to be ineffective. Merkulov [22] observed no prophylactic effect after the use of solution of calcium hydroxide U. S. P. and chlorinated lime. Livingston and Walker [13] found that hydrogen peroxide in 0.6 to 1.5 per cent concentration or bleaching powder (chlorinated lime) in 1 : 400 concentration damaged the normal cornea. Benzoyl peroxide in oily solution was found to be ineffective. Bickerton [38a] noted some irritation following the use of a 1 : 1,000 solution of sodium hypochlorite.

(*d*) Irrigating apparatus: Stallard [39] has devised a practical field container for irrigating fluids. Four perforated discharged bullet casings are soldered into the base of a 2 gallon petrol tin and connected by rubber tubing to irrigator nozzles. The tin is mounted on a standard which is inserted into the ground. The author also mapped a floor plan for use by attendants irrigating the eyes of gas casualties. With routine irrigation of each eye for one and one-half minutes, a team of four orderlies can treat 80 casualties per hour with one of these irrigating tins.

Livingston and Walker [13] described an efficient irrigating speculum (fig. 1; made by Down Brothers) with three arms, the irrigating fluid

38. Pellathy, B.: Versuche zur Minderung der Senfgaswirkung, Szemészet **74**:48, 1938; abstracted, Zentralbl. f. d. ges. Ophth. **43**:346, 1939. Lustig, A.: Effetti dei gas di guerra sull'occhio. Rivista sintetica, Boll. d'ocul. **13**:685, 1934; abstracted, Zentralbl. f. d. ges. Ophth. **32**:340, 1935. Whiting, M. H., and others: Discussion on Gas Injuries of the Eyes, Proc. Roy. Soc. Med. **33**:225, 1940. Heinsius.[37]

38a. Bickerton, R. E., in Discussion on Gas Injuries of the Eyes, Proc. Roy. Soc. Med. **33**:235, 1940.

39. Stallard, H. B.: Improvised Eye-Irrigator for Use in the Field, Brit. J. Ophth. **24**:53, 1940.

coming through perforations in these arms. In cases in which the edema of the lids and conjunctiva is marked, this speculum is said to make removal of the accumulated exudate more efficient.

Bradbury [40] described a type of eye cup irrigator which fits over the lids (fig. 2). Above there are an inlet nasally and an outflow temporally. The front contains a window glass through which the eye may be viewed during irrigation.

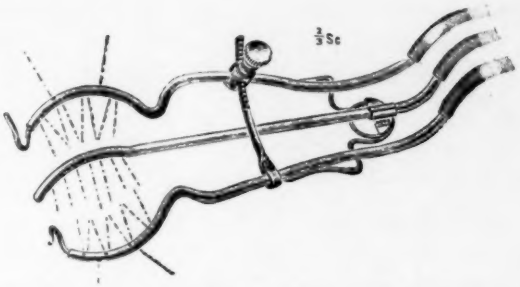


Fig. 1.—The irrigating speculum described by Livingston and Walker.

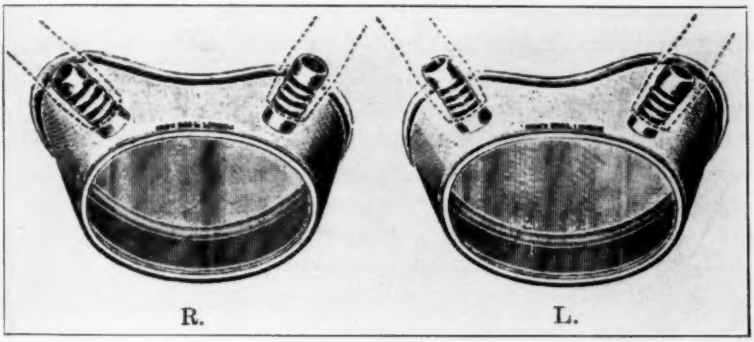


Fig. 2.—The eye cup irrigator described by Bradbury.

3. Dark Glasses or Eye Shade: Even though the mustard burn does not involve the cornea and secondarily the iris, there may be photophobia because of the extreme conjunctival irritation. The patient should be given dark glasses or an improvised eye shade for only a few days. Overemphasis on the seriousness of the lesion will delay the subjective cure.

4. Convalescence: Ophthalmologists universally recommend the following prescription for use during the convalescent period because of

40. Bradbury, S.: Decontamination of Eyes Which Have Been Contaminated by Mustard Gas, J. Roy. Nav. M. Serv. **22**:341, 1936.

the astringent and mildly antiseptic action of zinc sulfate in 0.25 per cent concentration:

Zinc sulphate	1 grain (0.06 Gm.)
Boric acid	10 grains (0.6 Gm.)
Epinephrine 1:1,000.....	1 drachm (3.7 cc.)
Distilled water.....	1 ounce (30 cc.)

Directions: 2 drops in each eye three times a day.

B. *Patients with Corneal Involvement.*—Although this group is small (less than 10 per cent of all patients with mustard gas injuries to the eyes), the severity of the symptoms, the prolonged convalescence and the frequent reduction in final vision demand the best efforts of the ophthalmologist.

1. Immediate Treatment: The first three procedures are identical with those for conjunctival involvement alone, viz.:

(*a*) Reassurance that the patient is not blind.

(*b*) Irrigations with boric acid, saline or sodium bicarbonate solution or with 0.5 per cent dichloramine-T in chlorinated paraffin. If necessary, 1 drop of isotonic pontocaine solution 0.5 per cent may be instilled to facilitate the opening of edematous lids.

(*c*) Use of dark glasses or eye shade: Several clinical reports have stressed the unfavorable effect of sleep on the ocular prognosis, and all criticize the use of bandages or eye pads. Closing the lids possibly aggravates a corrosive burn because of one of the following reasons: (1) accumulation of tears and exudate, (2) an increase in pressure on previously damaged and necrotic tissue and (3) an elevation in the temperature of the cornea.

(*d*) Atropine: Most patients with involvement of the cornea have photophobia, many with what must be reflex miosis. This is greatly alleviated by the use of atropine. Warthin and Weller [5] found that in rabbits and dogs one hundred and ten hours after the exposure to mustard the iris and ciliary body became infiltrated with polymorphonuclear cells. To counteract early reflex miosis and photophobia and to have the pupil well dilated before active iritis begins, atropine should be instilled routinely in all cases of corneal involvement. Either atropine sulfate solution 1 per cent or atropine ointment 1 per cent may be used at least once a day.

2. Oily Drops and Ointments: Many substances have been recommended for manifold purposes, most of the recommendations being poorly substantiated by experimental or clinical work. In general, oily drops and ointments are used (*a*) to lubricate the eye, thus preventing a sticky accumulation of exudate, with sealing of the lid margins; (*b*) to prevent later symblepharon; (*c*) to dissolve mustard and thus extract it from the tissues, and (*d*) to promote healing of the corneal epithelium.

Stallard [39] recommended the instillation of liquid paraffin just a few minutes before the first irrigation of the eye. Although this procedure may help to unseal the lids and lubricate tenacious exudate, it has not been demonstrated that oily drops will facilitate the removal of toxic substances when the eye is subsequently irrigated with immiscible aqueous solutions.

Symblepharon is a rare complication after mustard vapor burns. Clinically, only the exposed conjunctiva between the lids appears to be involved, showing an early yellowish white chemosis which becomes a horizontal band of hyperemia during the healing stage. The palpebral conjunctiva and the conjunctiva in the cul-de-sacs are relatively unaffected by mustard vapor. For this reason, adhesions between lids and globe are uncommon. In the rare cases of burns by liquid mustard, the conjunctiva in the cul-de-sacs is usually damaged and later symblepharon is common. If the patient gives a definite history of having been splashed with liquid mustard and the conjunctiva of the cul-de-sacs is found to be edematous or necrotic, the use of oily drops and the frequent breaking of adhesions with a glass rod is of course necessary. The official British treatment for all severe mustard burns [41] was to instill liquid paraffin drops three times a day. Castor oil was considered slightly irritating.

Although mustard is very soluble in oily solutions, the efficacy of oily drops or ointments in the removal and the neutralization of mustard is uncertain. Most writers agree that oily drops or ointments are to be avoided when the subject is still exposed to mustard vapor. They absorb and concentrate mustard gas in the eye. However, for use after removal of the patient from the vicinity of exposure, Rea [42] reported that the German Red Book of 1918 recommended a hydrous wool fat ointment with 10 per cent sodium bicarbonate as first aid treatment. Today the German Red Book recommends alkalinized cod liver oil with dextrose. Bonnefon [35] argued against the use of any type of oily drop or ointment because he believed that it retained mustard in the eye. Instead, as noted, he advised the use of hypertonic solutions to stimulate secretion of tears and withdraw fluid and toxic material from the tissues of the eye.

The use of lubricating ointments is thought to protect the damaged corneal epithelium and to promote its regeneration. The use of cod liver oil by the Germans is interesting in this respect. Whether the presence of vitamin A in the ointment increases the viability and the regeneration of the corneal epithelium is disputed. Livingston and Walker [13]

41. Gas Casualties: Manual of Treatment, Great Britain, War Department, London, His Majesty's Stationery Office, 1930.

42. Rea, L., in Discussion on Gas Injuries of the Eyes, Proc. Roy. Soc. Med. **33**:235, 1940.

found that 9 rabbits whose mustard burns were treated with cod liver oil showed marked improvement in healing over 1 control rabbit. The control rabbit did worse with liquid paraffin treatment than other rabbits with no treatment at all. However, as pointed out hereafter, Mann and Pullinger [6] found that the dose of mustard used in their experiments was variable.

3. Ascorbic Acid: Livingston and Walker [13] introduced this therapeutic prospect by their experiments on rabbits. They found that in 4 rabbits the daily intravenous injection of 500 mg. of neutralized ascorbic acid prevented the development of serious corneal opacities after approximately 0.085 cc. of liquid mustard had been instilled into the eyes. In 1 control rabbit, which received no ascorbic acid, severe lesions developed after the instillation of the same amount of mustard.

Mann and Pullinger [6] repeated these experiments using the same sample of mustard and found that with the method of instillation used by Livingston and Walker there were wide variations in the size of the initial abrasion and in the subsequent course of the burn. About half of the eyes showed a clinical cure after one week, i. e. subsidence of edematous clouding and early vascularization of the cornea. The other half continued to show clouding of the cornea with increasing vascularization for as long as three months. No essential difference in this ratio was found between 6 rabbits treated with 500 mg. of ascorbic acid injected intravenously every day and 6 control rabbits. In 4 additional rabbits these investigators carefully instilled 0.0005 cc. of liquid mustard by means of a calibrated Pasteur micropipet. In spite of the use of ascorbic acid, there were marked palpebral and conjunctival reactions for seven days, with clouding of the corneas, and by the twenty-first day all the corneas had vascularized. This course was similar to that described by Warthin and Weller [5] after the careful instillation of 0.0004 cc. of liquid mustard. Mann and Pullinger concluded that "the degree of damage is related to the dose and is not influenced by resistance of individual animals to the chemical. Identical doses produce almost identical lesions." The use of ascorbic acid injected intravenously had no beneficial effect on the course of the mustard burn.

4. Secondary Infections: The skin, eyes and respiratory tract all show a predisposition toward secondary infection after a mustard burn. This may be related to many factors previously discussed, viz.: (*a*) the large amount of tissue necrosis, which would afford a good bacteriologic medium; (*b*) damage to the bone marrow, with development of leukopenia in cases of severe involvement, and (*c*) a diminished capacity to produce circulating antibodies.

Bursuk [43] found that the introduction of pathogenic staphylococci into rabbits' eyes with mustard produced more destructive lesions than in control eyes. On the other hand, the instillation of mustard would sterilize a previously introduced culture of staphylococci.

(*a*) Mild silver protein and boric acid: During the first World War, instillation of mild silver protein in 2 to 10 per cent concentration followed by irrigation with boric acid solution was universally used to prevent or treat secondary infection. Mild silver protein is only slightly antiseptic and is used primarily to facilitate the removal of mucus and exudate when the eye is subsequently irrigated.

(*b*) Antiseptics: Many types of corneal abrasions and ulcerations are treated in some clinics with the instillation of acriflavine in castor oil 1:15,000. Other antiseptics in general use may prove equally efficacious.

(*c*) Sulfanilamide and derivatives: Within the past few years ophthalmologists have tried for local use in the eye many types of ointments prepared with sulfanilamide or a derivative. Guyton [44] said that sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) ointment (5 or 10 per cent) is probably more efficacious than the other sulfanilamide compounds in the treatment of corneal ulcers. He and other investigators have found that finely ground sulfathiazole in white petrolatum (5 per cent ointment) is probably equal to other more complicated preparations in the lack of irritation it causes and in therapeutic results. It appears certain that this ointment is beneficial for corneal ulcers, and either the sulfathiazole ointment or the petrolatum base alone appears to hasten the obtaining of negative cultures in some cases of conjunctivitis.

For panophthalmitis secondary to corneal ulceration the systemic use of sulfathiazole or sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) is recommended. The average dose by mouth is 0.1 Gm. per kilogram of body weight per day divided into six equal doses.

5. Convalescence: After two to three weeks, when the initial chemotic and exudative reaction has subsided, the use of zinc sulfate solution 0.25 per cent with epinephrine is generally recommended. As soon as there appears to be no more progression of the corneal lesion and the secondary iritis subsides, atropine should be discontinued. As soon as the pupil returns to normal size the dark glasses should be removed in spite of complaints of photophobia by the patient. This will aid in the prevention of chronic neurasthenic and hysterical reactions.

43. Bursuk, G. G.: Zur Frage der Infektion des mit Dichlordiäthylsulfid affizierten Auges, abstracted, Zentralbl. f. d. ges. Ophth. **36**:513, 1936.

44. Guyton, J. S.: Local Use of Sulfanilamide Compounds in the Eye, Am. J. Ophth. **24**:292, 1941; personal communication to the author.

At best the convalescence after a serious mustard burn of the cornea requires two or three months, and it is usually considered advisable to transport the patient to a convalescent home where psychiatric treatment is available. The local use of short wave diathermy will often speed up the reparative processes in the eyes.

6. Late Treatment: Few men were permanently blinded by mustard during the first World War, but the final vision of many was reduced by the irregular astigmatism or corneal opacification which remained. Irregularities in the corneal surface may often be corrected by a contact lens. The corneal lesion is said to improve in some cases after the irritation caused by fitting the contact lens.

Selected patients with greatly reduced vision because of corneal opacification may benefit from keratoplasty. Castroviejo [45] has enumerated the conditions which justify operative intervention. In general vision should be reduced below 20/100 in each eye, the cornea should not be entirely opaque or completely covered by a pannus of vessels, the anterior segment should be free of anterior synechias and there should be no evidence of glaucoma. This author has had great success with the square, penetrating type of graft, using a fine silk suture to hold the transplant in place.

VII. SUMMARY OF PRESENT TREATMENT

Even though the present treatment of mustard gas injuries to the eyes is largely symptomatic, the procedures used will help prevent the development of secondary complications. These methods may be summarized in the following chronologic sequence of treatment:

1. Reassurance of the patient that he is not blind by opening the swollen lids. Local anesthetics should be avoided because they damage the corneal epithelium. However, if necessary for examination of the patient, 1 drop of isotonic pontocaine solution 0.5 per cent may be instilled.

2. Immediate irrigation of each eye for two minutes with one of the following solutions: sodium bicarbonate 1.5 per cent, physiologic solution of sodium chloride, boric acid 2 per cent, or dichloramine-T 0.5 per cent in chlorinated paraffin.

3. In cases in which there is corneal involvement or marked photophobia, instillation of 1 per cent atropine solution or ointment every day until the symptoms or the iritis subsides.

4. In cases of severe involvement instillation of one of the following drops or ointments three times a day, not sooner than twenty-four

45. Castroviejo, R.: Keratoplasty, Am. J. Ophth. **24**:1 and 139, 1941.

hours after the exposure to mustard: liquid paraffin, cod liver oil with added sodium bicarbonate and dextrose or acriflavine in castor oil 1:15,000.

5. Use of dark glasses or a brown eye shade. These should be worn for the shortest possible time in order that the development of neurasthenic symptoms may be avoided. Bandages or eye pads should not be used.

6. Instillation of mild silver protein solution 10 per cent followed by irrigation with boric acid solution three times a day.

7. Use of zinc sulfate solution 0.25 per cent with epinephrine during convalescence.

8. Psychiatric care in a convalescent home if necessary.

Obituaries

JULIUS WOLFF, M.D.
1870-1942

Dr. Julius Wolff died of a heart attack at his residence, 1112 Park Avenue, New York, on January 26. He was 72 years old.

Dr. Wolff was born in New York city, attended the Sachs Collegiate Institute and was graduated from Harvard University in 1890 with the degree of A.B.; he then attended the Columbia University College of Physicians and Surgeons, New York, and received the degree of M.D. in 1893.

After an internship of two years in the Lenox Hill Hospital, he spent three years of postgraduate study in Strasbourg, Cologne, Paris and London and returned to New York in 1898 to engage in the practice of ophthalmology.

He was ophthalmologist at the Randall Island Hospital from 1899 to 1905, assistant ophthalmic surgeon at Bellevue Hospital from 1927 to 1932, attending ophthalmic surgeon and head of the department of ophthalmology at Mount Sinai Hospital from 1923 to 1932 and since then consulting ophthalmologist at the same institution. He was a member of the Medical Society of the State of New York, of his county medical society, of the American Medical Association and of the American Academy of Ophthalmology and Otolaryngology and a fellow of the New York Academy of Medicine and the American College of Surgeons. During the first World War he served as ophthalmologist for an army board of examiners; although his age precluded active service in the present war, he devoted much time to teaching first aid classes.

Dr. Wolff took an active part in the meetings of the New York Academy of Medicine, Section of Ophthalmology, and frequently made important clinical contributions. Among these might be mentioned "The Occurrence of Retraction Movements of the Eyeball Together with Congenital Defects in the External Ocular Muscles" (ARCH. OPHTH. **29:** 297, 1900); "A Conjunctival Apron or Safety Flap in Cataract Extraction: A Plea for Its Adoption as a Routine Procedure" (ibid. **52:** 554 [Nov.] 1923), and "A Sign in Differential Diagnosis of Lesions Producing Unilateral Exophthalmos" (*Am. J. Ophth.* **13:** 989 [Nov.] 1930).

Outside of his profession, Dr. Wolff had many and varied interests. He enjoyed outdoor sports, particularly golf; he loved music and was himself an accomplished cellist. His special hobby was wood carving, in which he showed extraordinary talent; some of his works were exhibited at the New York Academy of Medicine, receiving very favorable comment, and lately he donated a number of his sculptures to Bundles for Britain to be sold for war relief.

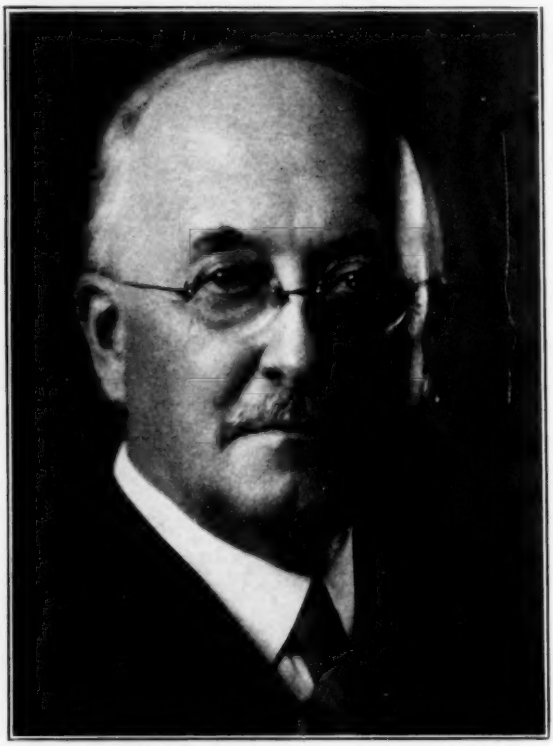
He enjoyed a large practice and was held in high esteem by his colleagues. Skill, honesty and amiability endeared him to his patients, the humblest of whom he treated with special kindness and consideration. His fine character was recognized by all with whom he came in contact.

He is survived by his wife, Mrs. Hilda Adler Wolff, and two daughters, Mrs. Jerome L. Strauss, of New York, and Mrs. Edmund J. Kahn, of Dallas, Texas.

CHARLES H. MAY.

EDWARD ADAMS SHUMWAY, M.D.
1870-1941

Edward Adams Shumway was born in Philadelphia Sept. 3, 1870, the son of Lowell Shumway, of Massachusetts, and Anna Bussier Shumway, of Philadelphia. His preliminary education was obtained in the public schools, terminating in 1887, when he graduated from the old Central High School. He then entered the University of Pennsyl-



EDWARD ADAMS SHUMWAY, M.D.
1870-1941

vania; he received the degree of bachelor of science from the College Department in 1891 and the degree of doctor of medicine from the School of Medicine in 1894. He interned at Blockley Hospital, now known as the Philadelphia General Hospital, and in 1897 commenced his special studies as a resident at the New York Eye and Ear Infirmary. Later he spent a year abroad, studying in Frankfort, Berlin and Vienna. On

his return to Philadelphia he entered the practice of ophthalmology, which he continued without interruption until his last day.

Dr. Shumway held a number of important appointments in the clinical field. He was ophthalmologist to the Hospital of the University of Pennsylvania and to the Childrens, Lankenau, Howard and Oncologic hospitals. He was an instructor in ophthalmology at the University of Pennsylvania School of Medicine from 1902 to 1921, when he became assistant professor of ophthalmology, resigning in 1923. He was a member of the American Medical Association and of his state and county societies, a fellow of the Philadelphia College of Physicians and a member of the American Ophthalmological Society. During World War I he conducted ocular examinations for the draft.

His fraternities were Phi Delta Theta and Alpha Mu Pi Omega (medical).

In 1901 Dr. Shumway married Annie Price, the daughter of Dr. and Mrs. Mordecai Price, of Philadelphia. He is survived by two sons: Norman, a physician, now in military service overseas, and Edward A. Jr., who is engaged in commercial pursuits.

In his earlier days Dr. Shumway devoted much of his attention to pathology and contributed pathologic studies to many papers in joint authorship with Dr. de Schweinitz and Dr. Posey.

He did not like teaching, however. In his later years he wrote very little and taught not at all. He was not interested in graduate teaching, which for the past twenty years or more has been the dominant factor in medical education and specialization. He was essentially a clinician, and throughout his professional life he practiced ophthalmology with learning and skill.

He was always kind, considerate and cooperative. He had a sense of humor when he cared to use it. He had no hobbies but at times played golf. He had the highest ideals and was an able ophthalmologist. In personal contact he was inclined at times to be shy and a little diffident.

WILLIAM T. SHOEMAKER.

Questions and Answers

To the Editor:—Would you be kind enough to help me with regard to a case of absence of the upper eyelashes? The patient is a girl 15 years old who apparently is in good physical condition but who has had a total absence of the upper eyelashes for the past six months. Occasionally the lashes grow ⅛ inch (0.3 cm.); then a white constriction of the ends appears and they drop out. There is no evidence of inflammation of the lid margins or of the conjunctivas. I have prescribed many types of vitamin capsules and also massage of the lids morning and evening with yellow mercuric oxide, after which heat has been applied for ten minutes.

S. H. R., M.D., South Carolina.

ANSWER.—When there is absence of the upper eyelashes without inflammation, one must consider the following factors:

1. Trichotillomania: The patient may pull out the lashes by the roots or close to the cutaneous surface involuntarily through habit. This condition is corrected through awareness of the patient of the neurosis. This mania for pulling out cilia is often associated with mental derangement.

2. Trichokryptomania: This is much like the aforementioned condition but signifies the secret self epilation of the cilia. The hairs are usually broken off close to the surface and may have constricted ends.

3. Trichorrhexis nodosa: This is usually found in the scalp, in the eyebrows and about the pubis. However, the eyelashes may be involved. Near the cutaneous surface there is usually a nodular thickening of the hair shaft, which breaks off, leaving a fibrillated end. The condition is treated by keeping the lid margins clean with green soap, each application being followed by thorough drying.

News and Notes

EDITED BY DR. W. L. BENEDICT, M.D.

UNIVERSITY NEWS

New Courses at New York University College of Medicine.—A basic science training course in ophthalmology is offered by the graduate department of ophthalmology at New York University College of Medicine. Dr. Daniel B. Kirby is the professor of ophthalmology, and Dr. Conrad Berens is the director of the course.

Nine months of intensive training in ophthalmology is given in preparation for a residency in ophthalmology in an approved hospital. The standards of the American Board of Ophthalmology were used as a guide in outlining the curriculum.

New courses instituted during the past year include pharmacology as a course separate from physiology and therapeutics, syphilis of the eye, medical ophthalmology and retinal physiology.

Among the new instructors are Dr. Edward Hartmann and Dr. Wendell Krieg.

Application blanks may be secured from the dean's office, New York University College of Medicine, 477 First Avenue, New York.

Achievement Award to Dr. William Thornwall Davis.—The Alumni Achievement Award of the George Washington University was given to Dr. William Thornwall Davis, of Washington, D. C., on June 6, 1941 for his outstanding work in organizing the postgraduate course in ophthalmology and that in aviation medicine. The latter course was the first of its kind and attracted worldwide attention.

SOCIETY NEWS

Reading (Pa.) Eye, Ear, Nose and Throat Society.—The seventh meeting, held at the Tyson-Schoener School Feb. 4, 1942, was called in order to acquaint the local ophthalmologists with the facilities and equipment of the sight-saving classes.

Information was presented concerning the educational management of children with visual and aural defects. The meeting was addressed by Dr. Pearl E. Hackman, district ophthalmologist; Dr. Thomas H. Ford, superintendent of the Reading School District, and Dr. Stanley Fink, principal of the Tyson-Schoener School.

The society held its eighth meeting in Philadelphia on February 18. Part of the program consisted of surgical and dry clinics at Jefferson Medical College Hospital and Wills Hospital. There followed lectures by Dr. Isaac S. Tassman on "Cross Cylinders," Dr. Louis Lehrfeld on "Ocular Allergy," Dr. Edmund B. Spaeth on "The Vertical Element in Lateral Muscle Imbalance" and Dr. S. G. Dublin on "Slit Lamp Microscopy." In the evening the members of the society attended the meeting of the Section on Otolaryngology of the Philadelphia College of Physicians.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Bacteriology and Serology

THE CULTIVATION OF CONJUNCTIVITIS- AND KERATITIS-PRODUCING AGENTS ON THE CHORIOALLANTOIC MEMBRANE OF CHICK EMBRYO. P. THYGESON, Am. J. Ophth. **23:** 1217 (Nov.) 1940.

From his studies Thygeson concludes that "egg-membrane cultures would appear to be of particular value in the study of suspected herpes or vaccinia and of suspected diplobacillary infection when ordinary culture methods have failed. They may also be found to be useful (1) in immunological studies of viruses and bacteria; (2) in the study of the phenomena of epithelial parasitism; and (3) in the maintenance of viruses and bacteria in a virulent condition." The author plans to consider these possible uses in a subsequent report. W. S. REESE.

Conjunctiva

ARGYROSIS OF CONJUNCTIVA, CORNEA AND TEAR-SAC. A. LOEWENSTEIN, Brit. J. Ophth. **25:** 360 (Aug.) 1941.

Loewenstein describes the histologic changes in the conjunctiva and in the tear sac in a case of extensive argyrosis involving the bulbar and the palpebral conjunctiva, the caruncle, the cornea and the tear sac. Nowhere in the conjunctiva or the tear sac was there a trace of silver within the epithelium. The silver deposits were situated predominantly in fibers and ribbons corresponding to the elastic system. Silver-stained fibers were far more frequent in the sac than in the conjunctiva. Silver particles were also found free in the tissue, sometimes in large clusters, and within the endothelial cells.

The author discusses the question of how the silver particles pass through the epithelial cell row. It may be that they are absorbed by the leukocytes which move actively through the epithelium into the subepithelial tissue, where they perish and liberate what they have engulfed. The selective staining of the elastic elements is probably a chemical reaction. W. ZENTMAYER.

Comparative Ophthalmology

AN INHERITED EYE DEFECT IN THE GUINEA PIG. H. L. FOUST, Am. J. Ophth. **23:** 1146 (Oct.) 1940.

This is the second report on anatomic studies of an inherited defect of the eye in the guinea pig and concerns the cornea almost exclusively. W. S. REESE.

Cornea and Sclera

HOMOTRANSPLANTATION OF PRESERVED CORNEA. M. FINE, Am. J. Ophth. **23:** 1140 (Oct.) 1940.

After reviewing the literature Fine describes his experiments on animals. For keratoplasty he used in one series corneal sections that

had been preserved for different lengths of time and in a second series perfectly fresh corneal tissue. From the results of this transplanting he concludes that fresh corneal tissue is superior for keratoplasty to corneal tissue preserved for more than twenty-four hours, while tissue preserved for twenty-four hours gives nearly as good results as fresh tissue.

W. S. REESE.

EPIDEMIC SUPERFICIAL PUNCTATE KERATITIS IN MALAYA. A. VISWALINGAM, Brit. J. Ophth. **25:** 313 (July) 1941.

This article is based on 3,521 cases observed in Selangor, one of the Federated Malay States, from 1935 to 1938. The special features of the sporadic form of the disease and of its later assumed epidemic type were as follows:

"1. Onset fairly sudden, sometimes a matter of a few hours.

"2. Invariably one eye is affected at first; the left eye in 962 cases and the right eye in 853 cases were affected.

"3. Cold weather and baths in pools appeared to bring about the onset and aggravate the symptoms.

"4. The reaction in some individuals is so severe as to give one the impression that a violent irritant was injected into the conjunctiva and subcutaneous tissues of the orbital and peri-orbital areas.

"5. The virulence of the reaction was often severe in the eye affected first, but occasionally worse in the fellow eye.

"6. The susceptibility to infection is great in eyes that were convalescing after trauma, either surgical or otherwise. There were also a few cases in which a patient having treatment for chronic trachoma (stage iii) developed this affection, which cleared up quickly without affecting the course of the trachomatous condition in any way.

"7. Invariably the seat of trouble was the muco-cutaneous junction along the margin of the lids, or the bulbar conjunctiva adjoining the outer canthus along the palpebral fissure."

The author concludes that "it might be useful to add that the designation 'superficial punctate keratitis' or 'keratitis diversiformis et uveitis anterior' would appear to be inappropriate as these do not define the primary condition, but serve to indicate its complication only. Our experience would seem to show that it is primarily a disease of the conjunctiva caused by an exogenous infection which according to its severity spreads to the lymphatic glands in one direction, and, in the other direction, to the adjacent tissues of the conjunctiva, involving the cornea and uvea, causing superficial or deep complications according to the depth to which the infection has travelled.

"'"Acute kerato-conjunctivitis of undefined origin" occasionally becoming epidemic' would seem more aptly to describe this clinical condition."

The article is illustrated.

W. ZENTMAYER.

MOLLUSCUM CONTAGIOSUM CORNEAE. R. SYSI, Acta ophth. **19:** 25, 1941.

A 3 year old child presented the typical nodular lesions of molluscum contagiosum on the skin of the cheek, forehead and upper lip and on the border of the left upper eyelid.

The left eye showed a slight pericorneal injection and a central area of corneal infiltration about 4 mm. in diameter. In the midst of this infiltration was an elevated nodule about 1.5 mm. in diameter with an umbilicated center. This was excised, together with the nodule on the eyelid. The nodule from the skin showed the typical picture of molluscum contagiosum; that from the cornea showed pigmented corneal cells suggestive of cells of molluscum contagiosum, but the small size of the specimen made a satisfactory histologic examination impossible.

O. P. PERKINS.

General

THE PROBLEM OF ASTHENOPIA. F. A. WILLIAMSON-NOBLE, Brit. J. Ophth. **25:** 397 (Sept.) 1941.

This lecture by Williamson-Noble does not lend itself to abstracting. The various causes of asthenopia are discussed, and emphasis is placed on the kinetic treatment of the eyes after the method of Stutterheim. The object of this treatment is to increase voluntary convergence.

The prolonged occlusion test of Marlow, as well as aniseikonia, is discussed.

W. ZENTMAYER.

General Diseases

RETINAL CHANGES WITH MARKED IMPAIRMENT OF VISION IN MEASLES. F. R. SHLOSSBERG and M. PRIZER, Am. J. Ophth. **23:** 998 (Sept.) 1940.

Shlossberg and Prizer report on a 6 year old girl in whom the vision in each eye was entirely lost five days after the onset of measles. Ophthalmoscopy revealed blurred disk margins with some swelling, moderately engorged veins and small and threadlike arteries. Throughout the fundi were numerous small round hemorrhages. Several months later there was postneuritic atrophy, a macular lesion was present, there were attenuated vessels in both fundi and the vision was 4/200 in the right eye and 3/200 in the left. No definite diagnosis was made, several ophthalmologists differing.

W. S. REESE.

General Pathology

GLASS MEMBRANES IN THE EYE. A. LOEWENSTEIN, Am. J. Ophth. **23:** 1340 (Dec.) 1940.

In this second and final article Loewenstein concludes that "the glass membranes as avascular colloidal tissue, fulfilling an important function, age much earlier than other tissues. Aging (histeresis) is a basic peculiarity of all colloids. Degeneration of the glass membranes is primarily the result of the physiological process of histeresis, but through other special influences, too (stretching through pathological growth, inflammation, systemic disease), their important function—the directed quantitative and qualitative filtration of the permeating fluids—may be destroyed. An exudate forms at the border of the glass membrane, very often with attraction of vessels, and there is new formation of young connective tissue—a degenerative pannus—a process well-known in the

cornea, and also in the lamina vitrea chorioideae. A systemic disease of all glass membranes of the eye is unknown up to the present day."

W. S. REESE.

Hygiene, Sociology, Education and History

STANDARDS FOR OUTPATIENT OPHTHALMOLOGIC DEPARTMENTS. C. BERENS, R. C. WILLIAMS and E. B. MERRILL, Am. J. Ophth. **23:** 1352 (Dec.) 1940.

Berens, Williams and Merrill give the following summary and conclusions:

"In this presentation of nursing and medical social service standards for eye clinics, standards are recommended for consideration in the establishment of eye clinics and departments. They should also aid in reorganizing present eye services.

"The committee is confident that the intelligent application of these standards will aid in preventing unnecessary blindness."

W. S. REESE.

Lacrimal Apparatus

ON THE HYPOFUNCTION OF THE LACRIMAL GLAND. A. DE RÖTTH, Am. J. Ophth. **24:** 20 (Jan.) 1941.

De Rötth gives the following summary of his observations:

"Attention is called to a certain group of patients, women in normal or artificial menopause, about 0.4 per cent of my eye cases, who suffer from light sensitiveness and burning of the eye; they become easily tired when reading and show practically no clinical symptoms. Their common symptom is very low lacrimal production. We consider these cases to differ only in degree from those of keratoconjunctivitis sicca and filamentous keratitis. They are the mildest form of the clinical manifestations of lacrimal hypofunction.

"Schirmer's method of checking the function of lacrimal gland by a strip of blotting paper has been standardized. It has been found that the lacrimal production decreases with the age. Above 40 years of age about one third of individuals have a lacrimal production that has been considered as pathologic by Schirmer, without offering any complaints because of the low secretion. Thus low secretion alone obviously does not always lead to filamentous keratitis. There are also other factors in play. Such factors might be, for example, disturbance of the trophic nerves of the cornea, ovarian hypofunction, vitamin-A deficiency, and a qualitative change in the tears."

W. S. REESE.

Lens

THE EVOLUTION OF LENS LESIONS IN EYE PERFORATIONS AND RUPTURES. M. DAVIDSON, Am. J. Ophth. **23:** 1358 (Dec.) 1940.

From a brief review of the literature and a survey of 62 cases, Davidson arrives at these conclusions:

"1. A survey of 62 lens lesions, primarily opacities, observed in cases of eye perforations by intraocular foreign bodies and in eye ruptures

without retention of foreign body, indicates that the majority are the result of lens contusion and morphologically belong to the type of contusion lens opacities previously studied. Posterior feathery star-shaped opacities are evidently rare.

"2. Capsule perforation, lens penetration, or its double perforation occur in less than a third of the cases that do not lead to immediate cataract.

"3. The retrospective diagnosis of the eye perforations or rupture origin of a lens opacity is sometimes made difficult because of the eventual blurring of the perforation or rupture character of a corneal scar after many years and particularly because of the difficulty in diagnosing an older partial limbus and scleral perforation or rupture.

"4. The rate of recession into the depth of the lens of originally subcapsular opacities is found to vary in this study just as in the study of pure contusion lens opacities. The factors affecting the rate seem to be: capsule lesions, which tend to retard it; varying depth of lens penetration, which would tend to accelerate it; hypertension and siderosis, which tend to retard it; and hypotension, which favors it.

"5. As to the evolution of the lens lesions in this mild variety of cases, the end results are satisfactory in the majority of cases, but prognosis should be more guarded in the individual after he is 30 years old. Deterioration should be watched for in the fifth decade, when apparently most deteriorations occur."

W. S. REESE.

HEREDITARY CATARACTA CAERULEA. O. R. WOLFE and R. M. WOLFE, J. Internat. Coll. Surg. **4:** 322 (Aug.) 1941.

The authors give—in three languages—the following summary of their report:

"Removal of soft cataracts by suction is an ideal method, as full restoration of vision is quickly obtained, it renders the usual needling operation obsolete and there is no disfigurement. Contact lenses can be comfortably worn after cataract surgery.

"Three cases of hereditary cataracta caerulea occurring in one family are reported. The condition was treated surgically in all three cases, with gratifying result."

W. ZENTMAYER.

Methods of Examination

CONCERNING THE CHAMBER ANGLE: III. A CLINICAL METHOD OF GONIOMETRY. H. S. GRADLE and H. S. SUGAR, Am. J. Ophth. **23:** 1135 (Oct.) 1940.

Gradle and Sugar present the following summary and conclusions based on their studies of normal and of glaucomatous eyes:

"1. We have described a new procedure, which we have termed goniometry, for measuring the acuity of the angle of the anterior chamber in the living eye.

"2. We have found that the acuity of the angle of the anterior chamber bears a gross but inconstant relationship to the depth of the

anterior chamber and is of greater value from a clinical standpoint than is the latter.

"3. Incidental to this study, the finding of Rosengren that a majority of cases of compensated glaucoma have chambers of normal depth, is corroborated.

"4. Clinical goniometry may be of value in following shallow-angle types of glaucoma and may indicate such normal eyes as should be watched for further evidences of impending glaucoma.

"5. It is suggested that goniometry be utilized in studying and evaluating provocative tests in preglaucomatous eyes." W. S. REESE.

Neurology

OCULAR SYMPTOMS IN FRACTURE OF THE SKULL. V. LARSEN, Nord. med. **8:** 2303 (Dec. 7) 1940.

Larsen reports 17 cases of fracture of the skull observed from three months to three years after the trauma from which ocular changes originated or were thought to have originated. The changes (except in cases of fracture of the frontal bone) were anomalies of refraction not previously recognized. In cases of fracture of the base of the skull in which there had been a lesion of the optic nerve, which is frequent, there were apparently characteristic defects in the field of vision in addition to the changes in the pupil characteristic of atrophy of the optic nerve: (1) limitation of the upper part of the field of vision; (2) limitation of the temporal part and (3) a central scotoma. The lower and nasal parts of the field were only slightly decreased. While the narrowing of the outer borders of the field apparently occurs directly after the lesion, some time seems to elapse before a central scotoma appears; so the latter is probably to be regarded as a result of the reparatory processes (yielding pressure on the optic nerve by the fibrous tissue, which, instead of callus, binds the cranial bones).

The author says that the diagnosis of fracture of the base of the skull can probably be made on the basis of this complex alone—central scotoma accompanied by severe defects in the upper and temporal parts of the field of vision. J. A. M. A. (W. ZENTMAYER).

Operations

KERATOPLASTY. R. CASTROVIEJO, Am. J. Ophth. **24:** 1 (Jan.) 1941.

Castroviejo briefly reviews the literature on keratoplasty, especially as it relates to his present technic, the development of which he outlines. He describes his present method in detail and also the postoperative care. A number of photographs showing clear square corneal transplants are shown. He claims that with this technic used in suitable cases 90 per cent or more of permanent transparencies may be expected.

W. S. REESE.

Pharmacology

A Comparative Study of the Effects of Mecholyl, Doryl, Eserine, Pilocarpine, Atropine, and Epinephrine on the Blood-Aqueous Barrier. K. C. Swan and W. M. Hart, Am. J. Ophth. **23:** 1311 (Dec.) 1940.

From their experiments on rabbits Swan and Hart arrive at the following conclusions:

"1. Inulin does not pass into the aqueous across the normal blood-aqueous barrier of rabbits, or does so only in faint traces. The administration of drugs that produce permeability of the blood-aqueous barrier to inulin also results in an increase in the solid constituents of the aqueous and a decrease in the latent period required for the passage of certain crystalloid dyes of varied electric charge. A mechanical decrease in the barrier between blood and aqueous is suggested as the explanation of these phenomena.

"2. Using the above criteria, the autonomic drugs can be classified according to their effects on the blood-aqueous barrier of the rabbit eye.

"(a) The effects of epinephrine [bitartrate] fall into two distinct phases. During the first hour (primary phase), there is no apparent effect on the barrier; but during the second and third hours (secondary phase), the permeability of the blood-aqueous barrier is increased.

"(b) Epinephrine (secondary phase, mecholyl [acetylbetamethylcholine], eserine [physostigmine salicylate] and doryl [carbaminoylcholine chloride] have the common property of increasing the permeability of the blood-aqueous barrier. In the concentrations used, mecholyl and eserine are most effective, and doryl least. The dye studies suggest that doryl may in some way increase the permeability of the iris vessels.

"(c) Pilocarpine [nitrate] acts as a weak miotic in albino rabbits and it is possible that its full ocular effects cannot be obtained in these animals. Studies with inulin and dyes provide no positive evidence that pilocarpine has any effect on the permeability of the blood-aqueous barrier. However, gravimetric experiments indicate that pilocarpine has the common property with epinephrine (secondary phase), mecholyl, doryl, and eserine of increasing the total solids of the aqueous.

"Atropine [sulfate] produces a slight decrease in the total solids of the aqueous, but without further investigation this cannot be attributed definitely to decreased permeability of the blood-aqueous barrier. The barrier remains impermeable to inulin, and the entrance of certain crystalloid dyes is not altered significantly.

"3. Changes produced in the blood-aqueous barrier by the autonomic drugs are not dependent on variations in the size of the pupil."

W. S. Reese.

Physiology

The Mechanism of the Intra-Ocular Pressure in Mammalia. T. Henderson, Brit. J. Ophth. **25:** 349 (Aug.) 1941.

Henderson gives the following summary of his interesting communication:

"(1) A series of problems, clinical and physiological, are enumerated which are inexplicable, if as alleged the intra-ocular pressure is two

and a half times greater than the intra-cranial pressure. They cease to exist with the realisation that the same mechanism and the same level of pressure, about 10 mm. Hg, obtain in the eye as in the brain.

"(2) The key to the understanding of the mechanism of the intra-ocular pressure is the reaction of the central retinal vein at the disk to the slightest touch on the lid, supplying clinical proof of the equilibrium between the intra-ocular pressure and venous exit pressure.

"(3) The intra-ocular pressure is not dependent on volume but, as in the brain, it is maintained and varies with venous exit pressure because this is the lowest circulatory pressure in the closed sphere of the globe.

"(4) It is the general circulatory pressure on the venous side which governs the physiological level of the intra-cranial and intra-ocular pressures and maintains them at 10 mm. Hg. Every variation in vena cava pressure is reflected backward millimetre for millimetre in both brain and eye. Variations in arterial pressure only produce a proportional change, as between the aorta and the venous exits in brain and eye the unknown and varying resistance of the arteries has to be overcome."

W. ZENTMAYER.

Retina and Optic Nerve

SUBJECTIVE "LIGHTNING FLASHES." R. F. MOORE, Am. J. Ophth. **23:** 1255 (Nov.) 1940.

After briefly reporting 33 cases, Moore gives the following summary:

"A symptom-complex is described which consists in the appearance of flashes of light, most frequently likened to lightning, seen to the temporal side of the eye, never to the nasal side, and vertical in direction.

"These flashes are accompanied by the simultaneous development of a crop of opacities in the vitreous. They seldom occur before middle age and are more frequent in the female sex. They do not imply any serious disease of the eye either at the time or subsequently."

W. S. REESE.

ANGIOMATOSIS RETINAE, WITH A REPORT OF FOUR CASES IN ONE FAMILY INVOLVING SIX EYES. L. STAZ, Brit. J. Ophth. **25:** 167 (April) 1941.

After a brief review of the literature Staz reports 4 cases of angiomatosis retinae in one family. A mother (aged 43), her daughter (aged 19) and her sons (aged 18 and 22, respectively) had the disease. In all, six eyes were involved. The mother, the daughter and the younger son were followed over five, one and seven years, respectively. The older son was seen but once. In none was there any sign of disease of the central nervous system or of other systems. The daughter, in whom the condition was advanced, was unsuccessfully treated by means of radium needles sutured to the exposed sclera in the region of the angioma.

The article is well illustrated.

W. ZENTMAYER.

SURGICAL CURE OF AN UNUSUAL DETACHMENT OF THE RETINA. E. C. ZORAB, Brit. J. Ophth. **25:** 229 (May) 1941.

The patient was a man aged 42. The left eyeball was phthisic after detachment of the retina. The right eye had high myopia. Vision was reduced to perception of hand movements in the extreme temporal periphery. The patient was flown to Utrecht, the Netherlands, where an operation was done by Weve. The resulting vision was 6/36 one year later.

According to Zorab, the main features of the case were the large size of the tear, which was more than half the circumference of the retina; the folding in half of the detached retina so that its posterior surface was facing anteriorly; the replacement of the retina by ordinary operation assisted perhaps by gravity but not by retinal hooks or other devices, and the degree of recovery of the vision after complete and wide separation of the macula for over a week.

W. ZENTMAYER.

INFECTION OF SPHENOIDAL SINUSES WITH SECONDARY AFFECTION OF THE EYES. E. W. ARNDT, Brit. J. Ophth. **25:** 324 (July) 1941.

The first case reported was that of a married woman aged 32 years. The vision failed rapidly without ophthalmoscopic changes. A diagnosis of retrobulbar neuritis was made.

After operation on the left sphenoidal sinus, which was found deeply congested, with a bead of pus showing, one short wave diathermy treatment was given. Two days later the retina in each eye was separated in the lower half of the fundus. Later the right sphenoidal sinus was opened and found congested. Diathermy was given to both eyes. The patient made an uneventful recovery, with spontaneous reattachment of the retina. The disks were yellowish red, and the macula showed points of exudation. Pigment spots were scattered throughout the retina.

The second case is that of an unmarried woman of 28 years. After a "cold" the left eye became blind. The optic disk was deeply congested, and the retinal veins were slightly distended. The sphenoidal sinuses were opened and found deeply congested; other therapeutic measures were also employed. Gradual recovery of vision followed.

W. ZENTMAYER.

DETACHMENT OF THE RETINA AND TRAUMA. H. FANTA, Klin. Monatsbl. f. Augenh. **105:** 30 (July) 1940.

Direct injury is recognized by most authors as a cause of detachment of the retina, whereas indirect trauma is not. This view supports Leber's idea that concussion of the eyeball but not concussion of the head may cause detachment of the retina. Fanta compiled the histories of 595 patients observed at the second ophthalmic clinic of the University of Vienna during the decade 1928 to 1938. Tables illustrate the findings. The author stresses the fact that none of his patients consulted the clinic with the intention of collecting indemnity or compensation for an accident. Injury was the probable cause of detachment of the retina in 100 eyes of 94 patients; it resulted in 9 per cent from a penetrating wound, in 46 per cent from a direct cause and in 38 per

cent from an indirect influence. Bodily overexertion was mentioned as the etiologic factor by 6 patients. The view of a number of writers is discussed, and a bibliography is appended.

K. L. STOLL.

A POSSIBLE EARLY FORM OF LEBER'S RETINAL DEGENERATION WITH MULTIPLE ANEURYSMS: REPORT OF A CASE. G. STROMBURG, Klin. Monatsbl. f. Augenh. **105:** 103 (July) 1940.

The author refers to the similarity of some symptoms of retinal degeneration with multiple aneurysms, described by Leber in 1912, to Coats's retinitis exsudativa and Hippel's angiomatosis. The morphologic changes are admittedly due to disturbances originating in the circulatory system. Early stages of Leber's retinal degeneration are reported rarely; 2 recent cases are briefly described. Stromburg adds the case history of a man aged 35. The report is illustrated with five photographs of the fundus. While the central portions of the retina were free from pathologic change, the peripheral arteries and arterioles showed multiple aneurysms at various stages. The development of aneurysms could be followed in some instances by daily ophthalmoscopic observations. No explanation could be given for the structure of the tegument of the aneurysms, which had the hue of mother-of-pearl and through which the dark red content could be noticed. There was insufficient material for histologic examination, and chemical examination of the blood furnished no clue.

The retinal changes always occurred unilaterally and in otherwise healthy men in the second or third decade of life. Obliterations had not yet formed at the early stage described. From the etiologic point of view some toxic process due to embolism was suspected. This theory was supported by the fact that overexertion preceded the onset of the visual disturbance. No source of focal infection could be found, and the weak positive reaction to tuberculin was not convincing evidence of tuberculosis. Pulmonary changes were absent. In this connection the author mentions that perivascular changes in tuberculosis may disappear without leaving a trace.

K. L. STOLL.

Tumors

BENIGN MELANOMAS OF THE CHOROID AND THEIR MALIGNANT TRANSFORMATION. E. A. ALBERS, Am. J. Ophth. **23:** 779 (July) 1940.

After reporting an illustrative case Albers presents these conclusions:

"It is quite evident that benign melanomas of the choroid are much more frequent than they were previously thought to be, occurring about once in 88 patients without complaints referable to the eye. Clinically a malignant melanoepithelioma is thought to have risen at the site of a previously benign tumor observed eight years previously on routine fundus examination. It is thought that melanomas as seen in the eye are usually benign, but that they may become highly malignant. Melanomas in the eye, once diagnosed, should be carefully watched for growth, which may be recognized by stippling or irregular pigmentation over the tumor. Should signs of growth become manifest, the eye should be immediately enucleated, for once the tumor gets so large that secondary glaucoma results, enucleation will usually not prevent early death of the patient from metastasis."

W. S. REESE.

METASTATIC CARCINOMA OF CHOROID WITH PRIMARY FOCUS IN THE PROSTATE GLAND. M. M. KULVIN, Am. J. Ophth. **23**: 892 (Aug.) 1940.

Kulvin reports a case and gives the following summary:

"There is presented a case of metastatic carcinoma of the choroid wherein the primary focus is considered to be presumably in the prostate gland.

"A complete search of the literature discloses only four other similar cases. The clinical diagnosis is confirmed by microscopic study of the eye."

W. S. REESE.

TUBERCULOMA OF THE EYE. G. E. DODDS, Brit. J. Ophth. **25**: 384 (Aug.) 1941.

The patient was a Yoruba boy 12 years of age. The globe, completely involved, was greatly enlarged. There was advanced spinal caries with spastic paralysis of the lower extremities. After three months of treatment the patient's general health had improved and the tumor of the eye diminished in size. The eyeball was enucleated. A soft solid mass which bore no resemblance to an eyeball, except for a remnant of the lens and cornea, it consisted of necrotic tissue bathed in creamy, yellow pus. Microscopically it was a mass of caseous tissue in which were numerous typical tuberculous giant cells. Direct smears failed to reveal tubercle bacilli, but a guinea pig inoculated with pus from the eye and killed after seven weeks showed typical tuberculous lesions containing acid-fast bacilli.

W. ZENTMAYER.

CLINICAL AND ANATOMIC OBSERVATIONS ON DRUSEN OF THE DISK AND THEIR COMBINATION WITH MELANOSARCOMA OF THE CHOROID: REPORT OF CASES. P. CIBIS, Klin. Monatsbl. f. Augenh. **105**: 78 (July) 1940.

Drusen of the disk were the only changes observed in a globe examined histologically for suspected melanosarcoma of the choroid. The patient, a woman aged 36, was under observation for about six years for nervousness, headaches, transient edema of the lids and blurred vision. The disks were somewhat pale and the margins not well outlined. The vision was normal, but the fields of vision showed enlargement of the blindspot and multiple small, scattered, absolute and relative scotomas for white. The surface of the disks was uneven owing to numerous drusen. A connection between the drusen and any ocular or general disease could not be established. Melanosarcoma was absent.

In the author's second case, a man aged 38 had drusen of the disk and a scantily pigmented melanosarcoma of the choroid. The disk was raised about 0.8 mm. above the level of the choroid. This prominence was due to a firm conglomerate of drusen which caused slight erosion of the lamina cribrosa. One third of the sclerochoroidal canal was filled with such conglomerates, which were more globular the smaller they were. They consisted of concentric layers which resembled those of "cerebral sand" in the hypophysis. Microchemical reactions showed them to resemble the hyalin described by von Recklinghausen.

The question is discussed whether hyalin may be the beginning stage of amyloid substances and whether amyloid substances may be retransformed into hyalin. Drusen of the optic nerve develop in cases of hereditary involvement when the optic nerve has been damaged by an analogous disposition or by a degenerative influence (yellow waxlike atrophy of the optic nerve). No connection between drusen and melanosarcoma appears to exist. The drusen cannot be senile formations: They were found in a child aged 9 years. On the other hand, examination of the eyes of 168 cadavers, 84 of which were of persons over 50 years of age, showed no indication of the formation of drusen.

K. L. STOLL.

LYMPHOBLASTOMA FOLLICULARE. J. GOEDBLOED and H. G. J. WŸERS, Acta ophth. **19:** 28, 1941.

The authors' summary is as follows:

In a man who thirteen years previously had suffered from swelling of the lymph glands of the groin and pelvis, which had undergone complete regression after several roentgen ray treatments, there developed at the age of 68, within a year, symmetric orbital tumors. On internal examination no swelling of lymph glands was found. The liver and the spleen were not enlarged. The blood picture was repeatedly found to be normal. After operative removal of the tumors, recurrences appeared in a few months, with retrobulbar extension and bilateral exophthalmos. The exophthalmos receded completely after roentgen ray treatments.

An extended description of the changes observed on histologic examination is given. The typical picture of lymphoblastoma folliculare was revealed. This disease has hitherto not been considered in the differential diagnosis of orbital lymphomas as mentioned in the opthalmologic literature.

O. P. PERKINS.

CORNEOSCLERAL CYST. M. VROLIJK, Acta ophth. **19:** 44, 1941.

A congenital epithelial cyst at the limbus corneae in a girl of 10 is described. Theories as to the origin of such cysts are discussed.

O. P. PERKINS.

Uvea

RECURRENT IRIDOCYCLITIS WITH HYPOPYON. R. SCHMIDT, Arch. f. Ophth. **142:** 185, 1940.

Of this rare and mysterious disease, which also goes under the names hypopyon iritis, hypopyon recidivans, iridocyclitis recidivans purulenta, iridocyclitis septica and ophthalmia lenta, the author reports 4 cases in which exhaustive clinical and pathologic studies were made without yielding definite clues with regard to the causation. Of repeated blood cultures only one showed Streptococcus viridans. The results of examination of the chest were considered insignificant by the consulting roentgenologist. In 2 cases the recurrences of the hypopyon were preceded by the development of aphthae on the mucous membrane of the mouth. Staphylococcus albus was grown from specimens of these aphthae. In

2 cases there was chronic pyoderma. There was no apparent relation between the recurrences of the cutaneous disease and those of the ocular disease.

In accordance with Urbanek's recommendation, blood transfusions were given in all 4 cases. The first transfusion had a marked beneficial influence, whereas the subsequent transfusions failed to prevent recurrences and to modify their course. All other therapeutic procedures (use of salicylates, fever therapy and chemotherapy) were of no avail. In 1 case the clinical condition improved slowly after combined treatment with sulfanilamide and germanin.

Two eyes became available for pathologic study. In the earlier stages of the disease perivascular inflammation was observed in the uvea and in the retina. In the later stages heavy membranes of inflammatory origin were the outstanding pathologic feature. P. C. KRONFELD.

Visual Tracts and Fields

CORTICAL HEMIANOPIAS. ESTEBAN ADROGUÉ, Arch. de oftal. de Buenos Aires **14:** 919 (Oct.) 1939.

Two cases of hemianopia due to a postgeniculate lesion are reported.

The first case was of transitory hemiplegia with accompanying nervous disturbances, in which incomplete hemianopia with neither alexia nor disturbance of orientation was observed, their absence indicating the Dejerine-Roussy thalamic syndrome. The status of the visual fields indicated preservation of the superficial layers of the cuneus, with a possible lesion of the deeper layers and of the lingual lobule. There was some preservation of the inferior quadrant.

In the second case the condition was of traumatic origin.

Reference is made to cases of Jacob and Fleischer.

C. A. FINLAY.

BITEMPORAL HEMIANOPIA FROM PRESSURE OF THE ANTERIOR CEREBRAL ARTERY. E. ADROGUÉ, Arch. de oftal. de Buenos Aires **14:** 999 (Dec.) 1939.

Adrogué reports on bitemporal hemianopia in a patient with a hypophysial adenoma and formation of a sulcus on the superior surface of the chiasma by pressure of the anterior cerebral artery. He then discusses anatomic and roentgenologic observations in cases of chiasmal compression.

C. E. FINLAY.

Sympathetic Ophthalmia

A CASE OF SYMPATHETIC OPHTHALMIA TREATED WITH SULFANILAMIDE. R. C. GAMBLE, Am. J. Ophth. **24:** 49 (Jan.) 1941.

Gamble reports the case of a boy with a perforating injury of the right eye in whom sympathetic ophthalmia developed. This had apparently improved with the use of sulfanilamide when the boy died from an accident. Pathologic examination of both eyes proved the diagnosis of sympathetic ophthalmia.

W. S. REESE.

Society Transactions

EDITED BY W. L. BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

ALGERNON REESE, M.D., *Chairman*

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April 21, 1941

Ocular Signs of Intracranial Saccular Aneurysms. DR. FRANK B. WALSH (by invitation) and DR. ARTHUR B. KING, Baltimore.

This article was published in full in the January 1942 issue of the ARCHIVES, page 1.

DISCUSSION

DR. R. TOWNLEY PATON: This is the first time that this subject has been presented before the Section of Ophthalmology. The paper contains numerous original observations, and the author should be commended for his excellent work. Jefferson insists on the ligation of the carotid artery in the treatment of intracranial aneurysms, and it seems to me that such ligation is logical and necessary. It is simpler and less dangerous than the "trap door" operation devised by Dr. Dandy. If there is no blood in the spinal fluid and the patient is in no immediate danger, would it not be safer to perform ligation before the "trap door" operation is considered?

DR. ISADORE GIVNER: A young man of 25 with complete paralysis of the left third nerve from infancy was recently seen in consultation with Dr. Raymond Meek. An operation for ptosis had been performed on two occasions, without appreciable improvement. The patient was unable to raise his left eyelid voluntarily, but partial elevation was elicited if he thought of sleep or if a bright light was flashed in his eye. Flashlight photographs were attempted, and it was found that the pupil became contracted and the eyelids separated. Although the patient has no other symptoms and feels comfortable, his condition fits into the picture described. Should surgical intervention be considered?

DR. CONRAD BERENS: Does ordinary encephalography help in the diagnosis?

DR. FRANK WALSH, Baltimore: Regarding the advisability of operation, the fact that in 1 case (case 10) the aneurysm existed for twenty years without surgical intervention is proof that operation is advisable. Richardson and Hyland do not advocate operation. Certainly our experience shows that surgical treatment is indicated in many cases.

Regarding operative intervention itself, I apparently did not make it clear that intracranial ligation and ligation of the internal carotid artery are often not performed at the same time. Whether they are depends on the patient's condition. In older patients the internal carotid artery is not completely tied off in the neck. There is often an interval of weeks between the ligation of the vessel in the neck and the intracranial operation.

Many points have come to light which may have an important bearing on poorly understood mechanisms such as cyclic oculomotor palsy and several curious pupillary phenomena.

Encephalography would undoubtedly show defects in the case of some large aneurysms, particularly those situated posteriorly. A crescentic shadow due to deposition of calcium in the aneurysmal wall is occasionally observed. In many cases which we have observed roentgen examination has given negative results. We have not had extensive experience in arteriography.

Photoreceptors of Vertebrates. DR. S. R. DETWILER (by invitation).

The comparative development of the retina and the optic nerve in vertebrates was discussed, and the lecture was illustrated by lantern projections.

DISCUSSION

DR. LEGRAND HARDY: This is the fundamental type of work with which advances are going to be made in the study of the physiology of the human retina, and I am most grateful to Dr. Detwiler for his presentation.

DR. ARTHUR ALEXANDER KNAPP: In both the chicken and the pigeon there is a pigmented band of tissue which extends from the optic nerve and the retina posteriorly, coming up anteriorly, attached to the retina along its course and apparently inserted into the region of the ciliary body. It comes up anteriorly through the vitreous and gives the appearance of a muscular structure. I wonder if Dr. Detwiler can provide enlightenment on that particular tissue.

DR. S. R. DETWILER: I am sorry that I do not know to what Dr. Knapp is referring. Has he any sections?

DR. ARTHUR ALEXANDER KNAPP: No. I have an accurate drawing.

DR. S. R. DETWILER: I am sorry that I have no information on the subject at the moment. With the aid of a section or a photograph, I might be able to answer the question.

Surgical Treatment of Orbital Plexiform Neurofibromatosis. DR. EDMUND B. SPAETH (by invitation), Philadelphia:

The author presented a brief review of plexiform neurofibromatosis, its evidence, its histopathology and the various anatomic defects associated with it. The anatomic defects discussed included such factors as ptosis and exophthalmos and such rare findings as retrobulbar aneurysm, sequestrum of the orbital rim and absence of one or more of the extraocular muscles.

A series of 11 cases were presented to illustrate the various surgical conditions which needed correction. The operations used were enumerated and pictures of the patients before and after the completion of surgical treatment shown.

DISCUSSION

DR. ALGERNON B. REESE: Dr. Spaeth has had wide experience with this type of case. One might think the condition had almost assumed epidemic proportions in Philadelphia. In any of the cases followed over a long period has there been any tendency for the tumor tissue to regrow?

DR. WENDELL L. HUGHES, Hempstead, N. Y.: Such cases are most disheartening. One obtains a fairly good result shortly after the operation, and later on the tumor tissue grows farther and one has another plastic job on one's hands. It is true of cases of this condition that, as some one has said, "once a plastic case, always a plastic case," and I have found such cases very discouraging.

DR. EDMUND B. SPAETH, Philadelphia: Dr. Hughes answered Dr. Reese's question. The tumor mass does recur. The patient who declined surgical intervention now has generalized sarcomatosis.

Case Reports

Lateral Proboscis with Demicyclopia. DR. RUDOLF AEBLI and DR. LOUISE MEEKER.

This article will be published in full in a later issue of the ARCHIVES.

DISCUSSION

DR. S. R. DETWILER: I wonder whether there are any other cases on record of unilateral cyclopia. Is this the only case reported? It appears most unusual to have the defect on one side, with the other side normal.

DR. ALGERNON B. REESE: Cyclopia is not difficult to explain, but three eyes are.

DR. S. R. DETWILER: It is difficult to understand this case embryologically. One can explain the median eye satisfactorily on embryologic grounds.

DR. LOUISE H. MEEKER: We have not fully exhausted the literature, but in the references we have looked up there are no other reports of patients with three eyes. Our studies are not completed.

DR. RUDOLF AEBLI: I am only sorry I did not remove the entire eye.

DR. ALGERNON B. REESE: Why wasn't the entire eye removed?

DR. RUDOLF AEBLI: I was afraid the child might die of meningitis due to the purulent condition described.

Marginal Dystrophy of the Cornea. DR. WILLIAM W. FITZGERALD (by invitation), Yonkers, N. Y.

A case of bilateral marginal degeneration of the cornea in a woman of 51 was reported. The complaints were redness of the right eye,

dull pain and blurred vision. Redness of the eye was first noted about three years previously.

There was a sheaf of dilated blood vessels between the caruncle and the limbus in the right eye. A yellow stripe of infiltrate extended from 1 to 5 o'clock just inside the nasal limbus. Below the superior limbus there was a narrow ectatic area. No other pathologic change was present.

A year later ectasia of a stripe of cornea below the upper limbus was marked, and a similar process was present in the left eye. The tension was 12 mm. of mercury (Schiøtz) in each eye. The visual acuity in the right eye was 6/9, with astigmatism against the rule. The visual acuity in the left eye was normal, without significant refractive error.

Book Reviews

The Modern Treatment of Syphilis. By Joseph Earle Moore, M.D. Second edition. Price, $7. Pp. 674. Springfield, Ill.: Charles C. Thomas, Publisher, 1941.

This edition has been rewritten and brought up to date with the aid of Dr. Jarold E. Kemp and the collaboration of Drs. Harry Eagle, Paul Padget and Mary S. Goodwin. Chapter III now deals with the infectiousness of syphilis and its relation to treatment. Two new chapters have been added, one on the intensive arsenotherapy of syphilis and one on the public health aspects of the treatment of syphilis.

As the first edition of this book was not reviewed in these ARCHIVES, it seems appropriate to draw attention to Section XX, on the treatment of ocular syphilis, which is of particular interest to ophthalmologists. It is conceded that the proper management of ocular syphilis demands the combined efforts of ophthalmologist and syphilologist. According to the author, the ophthalmologist's fear of arsenical drugs is ill founded, and his skepticism as to the results of treatment in interstitial keratitis and optic nerve atrophy are not justified. As has been shown by Zimmermann, the arsphenamines have no deleterious effect on the eye. While the direct and indirect effects may be classified as (1) true toxic reactions, (2) ocular therapeutic shock (the Jarisch-Herxheimer reaction) and (3) ocular relapses, these lesions, as the author says, are due not to the arsenical drugs but to too little of them. The treatment of iritis of chronic relapsing chorioretinitis and of optic nerve atrophy are taken up in turn; the discussion of the last, based on a large material studied in conjunction with the staff of the Wilmer Ophthalmological Institute, is particularly to be commended. An important chapter is that on interstitial keratitis, and in the discussion of its treatment the work of Klauder and Vandoren is especially praised.

We are indebted to Dr. Moore and his collaborators for an excellent presentation of an important subject, which, should be available to every medical practitioner.

ARNOLD KNAPP.

CORRECTION

In the abstract of discussion following the article by Dr. Alfred Cowan and Bernice C. English, "Causes of Blindness in Pennsylvania: An Analysis of a Group of Over Thirty Thousand Blind Eyes," which appeared in the November issue (**26:** 797, 1941), the last three paragraphs on page 805, beginning "His criticism of the type of detail," belong to the remarks made by Dr. Conrad Berens and should be transposed to page 806 after the paragraph beginning "He criticizes the length of the committee's classification."

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Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Ralph A. Fenton, 1020 S. W. Taylor St., Portland, Ore.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.
Place: Portland, Ore. Time: May 11-14, 1942.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Spencer S. Howe, 103 E. Holly St., Bellingham, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 419 Stimson Bldg., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. H. Elmer, 321 W. State St., Rockford, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Davis, 1615 Howard St., Omaha.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. L. Chester McHenry, Medical Arts Bldg., Oklahoma City.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.
Place: Richmond, Va. Time: November 1942.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.
Place: Albuquerque, N. Mex. Time: November 1942.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. H. Bailey, 29 S. Oakland Ave., Sharon.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Edward N. DeWitt, 836 Myrtle Ave., Bridgeport.
Secretary-Treasurer: Dr. Henry L. Birge, 179 Allyn St., Hartford.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Henry N. Blum, 912 American Bank Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOY AND OTOLARYNGOLOGY

President: Dr. Erling Wilhelm Hansen, 78 S. 9th St., Minneapolis.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. William J. Marshall, 335 Owen St., Missoula.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY, OTOLOGY AND RHINOLARYNGOLOGY

Chairman: Dr. Edgar P. Cardwell, 47 Central Ave., Newark.
Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. M. R. Gibson, Professional Bldg., Raleigh.
Secretary: Dr. Vanderbilt F. Couch, 105 W. 4th St., Winston-Salem.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. A. E. Spear, Dickinson.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.
Place: Columbia. Time: November 1942.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. E. L. Goar, 1300 Walker Ave., Houston.
Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. Everett B. Muir, Boston Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Earl H. Phillips, 623 Judge Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. Ferguson, Second National Bldg., Akron, Ohio.
Secretary-Treasurer: Dr. D. F. Mathias, First Central Tower, Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m. fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.
Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Meyer H. Riwchun, 367 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Sanford Gifford, 720 N. Michigan Ave., Chicago.
Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. W. J. Abbott, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. L. V. Johnson, 2065 Adelbert Rd., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. L. A. Nelson, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. S. F. Harrington, 921 Medical Arts Bldg., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Harvey E. Dowling, 2414 Eaton Tower, Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. James M. Dunn, 1352 Union St., Schenectady.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Felician J. Slataper, 1110-1111 Medical Arts Bldg., Houston, Texas.
Secretary: Dr. Theo. L. Holland, 611 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. John I. Garret, 57 Stokes Bldg., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.
Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. John Osburn, 523 W. 6th St., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.
Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenendoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.
Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. John W. Truitt, 161 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Kaufman Schlivek, 1016–5th Ave., New York.
Secretary: Dr. Brittain Payne, 896 Madison Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. James W. Smith, 1016–5th Ave., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. R. E. Leatherock, Cushing, Okla.
Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Harold Gifford, 1620 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.
Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

Chairman: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Secretary: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Clyde Markel, 200–9th St., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. James E. Landis, 232 N. 6th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. E. J. Avery, 11 N. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. William M. James, 508 N. Grand Blvd., St. Louis.
Secretary: Dr. H. Rommel Hildreth, 823 Metropolitan Bldg., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Fred Boyle, 490 Post St., San Francisco.
Secretary: Dr. Frank Hand, 450 Sutter St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Roy Seeley Moore, 1704 State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. John D. Skow, 2001 Collingwood Blvd., Toledo, Ohio.
Secretary: Dr. S. H. Patterson, 125–15th Ave., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. E. Leonard Goodman, 1801 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Sterling Bockoven, 1752 Massachusetts Ave. N. W., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.